## => file reg

FILE 'REGISTRY' ENTERED AT 09:45:54 ON 05 JUL 2001 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2001 American Chemical Society (ACS)

4 JUL 2001 HIGHEST RN 344549-73-1 STRUCTURE FILE UPDATES: DICTIONARY FILE UPDATES: 4 JUL 2001 HIGHEST RN 344549-73-1

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d his

L1

(FILE 'HOME' ENTERED AT 09:37:40 ON 05 JUL 2001)

FILE 'REGISTRY' ENTERED AT 09:38:14 ON 05 JUL 2001

E WAY124/CN E WAY 124/CN

1 S E6

E RAP.PA/CN

L2 1 S E2

E GP11044/CN

E GP 11044/CN

E RAP-PA/CN

E GPI 1044/CN

L3 1 S E3

SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:45:54 ON 05 JUL 2001

=> d l1; d l2; d l3

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ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
L1
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RN 149438-31-3 REGISTRY

27,31-Epoxy-5,36-etheno-1H,5H-pyrido[2,1-c][1,2,4]triazolo[1,2-CN q][1,4,17,18]oxatriazacyclohentriacontine-1,3,9,15,19,25,26(2H,6H,10H,19aH )-heptone, 7,8,11,14,16,17,20,21,22,23,27,28,29,30,31,32,33,36octadecahydro-11,27-dihydroxy-17-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3methoxycyclohexyl]-1-methylethyl]-10,33-dimethoxy-6,8,12,14,28,34hexamethyl-2-phenyl-, (6S,8R,10R,11R,12E,14R,17S,19aS,27R,28R,31S,33S,34E)-(CA INDEX NAME) (9CI)

OTHER CA INDEX NAMES:

27,31-Epoxy-5,36-etheno-1H,5H-pyrido[2,1-c][1,2,4]triazolo[1,2q][1,4,17,18]oxatriazacyclohentriacontine-1,3,9,15,19,25,26(2H,6H,10H,19aH )-heptone, 7,8,11,14,16,17,20,21,22,23,27,28,29,30,31,32,33,36octadecahydro-11,27-dihydroxy-17-[2-(4-hydroxy-3-methoxycyclohexyl)-1methylethyl]-10,33-dimethoxy-6,8,12,14,28,34-hexamethyl-2-phenyl-, [6S-[6R\*,8S\*,10S\*,11S\*,12E,14S\*,17R\*[S\*(1R\*,3S\*,4S\*)],19aR\*,27S\*,28S\*,31R\* ,33R\*,34E]]-[partial]-

OTHER NAMES:

WAY 124466 CN

FS STEREOSEARCH

MF C59 H84 N4 O15

SR CA

CA, CANCERLIT, CAPLUS, MEDLINE, TOXLINE, TOXLIT, USPATFULL LC STN Files: KATHLEEN FULLER EIC1700 308-4290

Absolute stereochemistry. Double bond geometry as described by E or Z. Currently available stereo shown.

PAGE 1-A

PAGE 2-A

11 REFERENCES IN FILE CA (1967 TO DATE)

11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS L2

RN 165047-17-6 REGISTRY

Glycine, (2S)-1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(2S,3S)-3-[(2S,3S)-3-[(2S,3S)-3-[(2S,3S)-3-[(2S,3S)-2-[(2S,CN 2-methoxybutyl]-3-methyl-2H-pyran-2-yl]acetyl]-2-piperidinecarbonyl-(.alpha.R)-.alpha.-aminobenzenebutanoylglycyl-N-methyl-,

(4.fwdarw.16)-lactone (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Glycine, N-[[1-[oxo[tetrahydro-2-hydroxy-6-(3-hydroxy-2-methoxybutyl)-3methyl-2H-pyran-2-yl]acetyl]-2-piperidinyl]carbonyl]-4-phenyl-D-2aminobutanoylglycyl-N-methyl-, .tau.-lactone, [2R-

[2.alpha.,2(S\*),3.alpha.,6.beta.(2S\*,3S\*)]]-

OTHER NAMES:

CN Rap Pa

FS STEREOSEARCH

MF C34 H48 N4 O10

SR

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.

7 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 190444-03-2 REGISTRY

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester, (S)-

OTHER NAMES:

CN GPI 1044

FS STEREOSEARCH

MF C33 H37 N O4

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.

- 4 REFERENCES IN FILE CA (1967 TO DATE)
- 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

## => file hcaplus

FILE 'HCAPLUS' ENTERED AT 09:46:57 ON 05 JUL 2001 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1947 - 5 Jul 2001 VOL 135 ISS 2 FILE LAST UPDATED: 4 Jul 2001 (20010704/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

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=> s 11 or 12 or 13
             11 L1
              7 L2
              4 L3
             18 L1 OR L2 OR L3
L4
    s 14 and hair
         37716 HAIR
              4 L4 AND HAIR
L5
=> d 15 all 1-4 hitstr
     ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
L.5
     2001:131200 HCAPLUS
AN
DN
     134:168380
     Small molecule pipecolic acid derivative hair growth
TI
     compositions and uses
     Steiner, Joseph P.; Hamilton, Gregory S.
IN
     GPI NIL Holdings, Inc., USA
PA
     U.S., 17 pp., Cont.-in-part of U.S. 5,945,441.
SO
     CODEN: USXXAM
DT
     Patent
LA
     English
IC
     ICM A61K031-55
NCL
     514211000
      63-6 (Pharmaceuticals)
CC
     Section cross-reference(s): 62
FAN. CNT 6
     PATENT NO.
                       KIND
                             DATE
                                            APPLICATION NO.
                                                              DATE
                             20010220
                                             US 1998-89373
     US 6191125
                        В1
                                                              19980603
PT
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                        Α
                             19990831
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                        Α
                             19981204
                        В1
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                                             US 1999-369860
                                                              19990809
     US 6239164
PRAI US 1997-869426
                        A2
                             19970604
     MARPAT 134:168380
OS
AB
     This invention relates to pharmaceutical compns. and methods for treating
     alopecia and promoting hair growth using pipecolic acid derivs.
     Efficacy of GPI 1044 (a pipecolic acid deriv.) in promoting hair
     growth in mice was shown. A lotion contained 95% ethanol 80.0, a
     pipecolic acid deriv. 10.0, .alpha.-Tocopherol acetate 0.01, ethylene
     oxide (40 mol) adducts of hardened castor oil 0.5, purified water 9.0,
     perfume and dye q.s. 100%.
     pipecolic acid deriv hair growth promoter
ST
IT.
     Proteins, specific or class
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (FKBP (FK 506-binding protein); small mol. pipecolic acid deriv.
      hair growth compns. and uses)
ΙT
      Alopecia
         (areata; small mol. pipecolic acid deriv. hair growth compns.
         and uses)
IT
      Drug delivery systems
         (emulsions; small mol. pipecolic acid deriv. hair growth
         compns. and uses)
IT
      Hair preparations
         (growth stimulants; small mol. pipecolic acid deriv. hair
         growth compns. and uses)
IT
      Drug delivery systems
         (lotions; small mol. pipecolic acid deriv. hair growth
```

KATHLEEN FULLER EIC1700 308-4290

```
compns. and uses)
IT
     Alopecia
        (male pattern; small mol. pipecolic acid deriv. hair growth
        compns. and uses)
ΙT
     Drug delivery systems
        (ointments, creams; small mol. pipecolic acid deriv. hair
        growth compns. and uses)
ΙT
     Alopecia
     Shampoos
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
ΙT
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
IT
     535-75-1D, Pipecolic acid, derivs.
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
                         186834-77-5, GPI 1102
                                                   186834-82-2, GPI 1116
IT
     104987-11-3, Fk506
                             212607-81-3, GPI 1206
     190444-03-2, GPI 1044
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
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(6) Anon; EP 88350 1983 HCAPLUS
(7) Anon; EP 196841 1986 HCAPLUS
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(28) Anon; EP 572365 1993 HCAPLUS
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(30) Anon; EP 0823419 1997 HCAPLUS
(31) Armistead; US 5192773 1993 HCAPLUS
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KATHLEEN FULLER EIC1700 308-4290

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(63) Ok; US 5208241 1993 HCAPLUS
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(66) Proctor; US 5714510 1998 HCAPLUS
(67) Rinehart; US 5294603 1994 HCAPLUS
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(69) Schreiber; US 5447915 1995 HCAPLUS
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(71) Sharpe; US 5631017 1997
(72) Sharpe; US 5703088 1997 HCAPLUS
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(74) Skotnicki; US 5252579 1993 HCAPLUS
(75) Takeuchi; US 5359138 1994 HCAPLUS
(76) Winkley; US 4438031 1984 HCAPLUS
(77) Zelle; US 5543423 1996 HCAPLUS
     190444-03-2, GPI 1044
TT
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
RN
     190444-03-2 HCAPLUS
CN
     2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-
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phenylpropyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
L5
     2001:111510 HCAPLUS
ΑN
DN
     134:168053
     Pipecolic acid derivatives for hair growth compositions and uses
ΤI
    Steiner, Joseph P.; Hamilton, Gregory S.
IN
PA
     Gpi Nil Holdings, Inc., USA
SO
     U.S., 29 pp.
     CODEN: USXXAM
DT
     Patent
LA
     English
IC
     ICM A61K031-44
NCL
     514291000
     62-3 (Essential Oils and Cosmetics)
CC
     Section cross-reference(s): 1
FAN.CNT 1
                                           APPLICATION NO. DATE
                     KIND DATE
     PATENT NO.
                           -----
                                           _____
                     ____
     _____
                     B1 20010213
                                           US 1998-89376 19980603
     US 6187784
PT
     This invention relates to compns. and methods for treating alopecia and
AΒ
     promoting hair growth using pipecolic acid derivs. Thus a
     lotion contained a pipecolic acid deriv. 0.05, hinokitiol 0.01,
     ethoxylated castor oil 0.5, water 19.0, perfume and dye qs and EtOH to
     80.0%.
    pipecolic acid hair growth; alopecia pipecolic acid hair
ST
ΙT
     Proteins, specific or class
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (FKBP-12 (FK 506-binding protein, 12,000-mol.-wt.); pipecolic acid
        derivs. for hair growth compns.)
     Hair preparations
ΤТ
        (creams; pipecolic acid derivs. for hair growth compns.)
ΤТ
     Hair preparations
        (emulsions; pipecolic acid derivs. for hair growth compns.)
     Hair preparations
ΤТ
        (growth stimulants; pipecolic acid derivs. for hair growth
        compns.)
IT
     Hair preparations
        (lotions; pipecolic acid derivs. for hair growth compns.)
IT
     Alopecia
     Shampoos
        (pipecolic acid derivs. for hair growth compns.)
ΙT
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (pipecolic acid derivs. for hair growth compns.)
ΙT
     53123-88-9, Rapamycin
                           141084-63-1
                                           147438-30-0
                                                         147438-31-1
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     148493-28-1 149438-31-3, Way 124466
                   152754-37-5
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     152754-36-4
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                                 153011-31-5, SLB 506
     152754-41-1
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                                               186960-09-8
                                                             252002-58-7
                   259225-69-9
                                 259225-71-3
                                               325685-52-7
     259225-63-3
     RL: BAC (Biological activity or effector, except adverse); BUU (Biological
     use, unclassified); BIOL (Biological study); USES (Uses)
        (pipecolic acid derivs. for hair growth compns.)
RE.CNT 231
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RE
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(33) Anon; EP 468339 1992 HCAPLUS
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(35) Anon; WO 9203472 1992 HCAPLUS
(36) Anon; WO 9204370 1992 HCAPLUS
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(48) Anon; WO 9314072 1993 HCAPLUS
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(69) Anon; WO 9615101 1996 HCAPLUS
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(71) Anon; WO 9633184 1996 HCAPLUS
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(84) Armistead; US 5192773 1993 HCAPLUS
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Absolute stereochemistry.

Double bond geometry as described by E or Z.

Currently available stereo shown.

PAGE 1-A

PAGE 1-B

PAGE 2-A

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Absolute stereochemistry.

L5

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ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
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     Small molecule pipecolic acid derivative hair growth
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     Hamilton, Gregory S.; Steiner, Joseph P.
IN
     Guilford Pharmaceuticals Inc., USA
PA
     PCT Int. Appl., 62 pp.
SO
     CODEN: PIXXD2
DT
     Patent
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     English
     ICM A61K007-48
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                              KATHLEEN FULLER EIC1700 308-4290
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PRAI WO 1998-US11264
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OS
     This invention relates to topical compns. and methods for treating
AΒ
     alopecia and promoting hair growth using pipecolic acid derivs.
     For example, 4-phenyl-1-(3-phenylpropyl)butyl 1-(3,3-dimethyl-2-
     oxopentanoyl)-2-piperidinecarboxylate and 1-phenethyl-3-phenylpropyl-1-
     (3,3-dimethyl-2-oxopentanoyl)-2-piperidinecarboxylate showed hair
     revitalizing properties in C57 black mice.
ST
     piperidinecarboxylate deriv alopecia treatment; hair growth
     promoter pipecolate deriv
IT
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (affinity to; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (creams; pipecolic acid derivs. for hair growth compns.)
IΤ
     Hair preparations
        (emulsions; pipecolic acid derivs. for hair growth compns.)
TT
     Hair preparations
        (growth stimulants; pipecolic acid derivs. for hair growth
        compns.)
IT
     Hair preparations
        (lotions; pipecolic acid derivs. for hair growth compns.)
TΤ
     Alopecia
     Shampoos
        (pipecolic acid derivs. for hair growth compns.)
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(1) Fujisawa Pharm Co, Ltd; EP 0423714 A 1991 HCAPLUS
(2) Guilford Pharm Inc; WO 9813343 A 1998 HCAPLUS
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RN
CN
     2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-
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Absolute stereochemistry.

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     Pipecolic acid derivatives for hair growth compositions
TΙ
     Hamilton, Gregory S.; Steiner, Joseph P.
IN
PA
     Guilford Pharmaceuticals, Inc., USA
SO
     PCT Int. Appl., 103 pp.
     CODEN: PIXXD2
DΨ
     Patent
LA
     English
     ICM A61K007-48
IC
     ICS A61K031-50; A61K031-435; A61K031-445; C07K005-02; C07K005-08
     62-3 (Essential Oils and Cosmetics)
CC
     Section cross-reference(s): 63
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PRAI WO 1998-US11242
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                            19980603
     This invention relates to pharmaceutical compns. and methods for treating
AΒ
     alopecia and promoting hair growth using pipecolic acid derivs.
     Thus, a hair lotion contained 95% EtOH, a pipecolic acid deriv.
     such as 4-(4-methoxyphenyl)butyl 1-(2-oxo-2-phenylacetyl)-2-
     piperidinecarboxylate 10.0, .alpha.-tocopherol acetate 0.01, ethoxylateed
     hardened castor oil 0.5, and water 9.0%, and perfume and dye.
     pipecolic acid deriv hair growth
ST
IT
     Hair preparations
        (creams; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (emulsions; pipecolic acid derivs. for hair growth compns.)
TΤ
     Hair preparations
        (growth stimulants; pipecolic acid derivs. for hair growth
        compns.)
     Hair preparations
IT
        (lotions; pipecolic acid derivs. for hair growth compns.)
IT
     Alopecia
     Immunosuppressants
                              KATHLEEN FULLER EIC1700 308-4290
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```
Shampoos
        (pipecolic acid derivs. for hair growth compns.)
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     Immunophilins
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(1) Armistead, D; US 5620971 A 1997 HCAPLUS
(2) Astra Aktiebolaget; WO 9611943 A 1996 HCAPLUS
(3) Fujisawa Pharm Co Ltd; EP 0423714 A 1987 HCAPLUS
(4) Guilford Pharm; WO 9813343 A 1998 HCAPLUS
(5) Nelson, F; US 5385908 A 1995 HCAPLUS
(6) Skotnicki, J; US 5252579 A 1993 HCAPLUS
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     q][1,4,17,18]oxatriazacyclohentriacontine-1,3,9,15,19,25,26(2H,6H,10H,19aH
     )-heptone, 7,8,11,14,16,17,20,21,22,23,27,28,29,30,31,32,33,36-
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     methoxycyclohexyl]-1-methylethyl]-10,33-dimethoxy-6,8,12,14,28,34-
     hexamethy1-2-pheny1-, (6S,8R,10R,11R,12E,14R,17S,19aS,27R,28R,31S,33S,34E)-
      (9CI) (CA INDEX NAME)
Absolute stereochemistry.
Double bond geometry as described by E or Z.
```

Currently available stereo shown.

PAGE 1-A

PAGE 1-B

PAGE 2-A

## => file reg

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FILE COVERS 1947 - 5 Jul 2001 VOL 135 ISS 2 FILE LAST UPDATED: 4 Jul 2001 (20010704/ED)

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=> d que 115

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GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

5607 SEA FILE=REGISTRY SSS FUL L6 T.10 4333 SEA FILE=HCAPLUS ABB=ON L10 L11

20 SEA FILE=HCAPLUS ABB=ON L11(L)(HAIR OR ?ALOPEC?) L15

=> d 115 1-20 all hitstr

ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2001 ACS L15

AN 2001:131200 HCAPLUS

DN 134:168380

Small molecule pipecolic acid derivative hair growth compositions and uses TΙ

Steiner, Joseph P.; Hamilton, Gregory S. GP,I NIL Holdings, Inc., USA ΙN

PΑ

U.S., 17 pp., Cont.-in-part of U. S. 5,945,441. SO

CODEN: USXXAM

DT Patent

English LA

ICM A61K031-55 IC

NCL 514211000

63-6 (Pharmaceuticals)

Section cross-reference(s): 62

FAN.CNT 6

11111.0111.0						
		PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	ΡI	US 6191125	В1	20010220	US 1998-89373	19980603
		US 5945441	A	1,9990831	US 1997-869426	19970604
		ZA 9804621	Α	19981204	ZA 1998-4621	19980529
		ZA 9804778	Α	19981204	ZA 1998-4778	1.9980603
		ZA 9804783	Α	19981204	ZA 1998-4783	19980603
		US 6239164	B1	20010529	US 1999-369860	19990809
	PRAI	US 1997-869426	A2	19970604		

OS MARPAT 134:168380

This invention relates to pharmaceutical compns. and methods for treating AΒ alopecia and promoting hair growth using pipecolic acid derivs. Efficacy of GPI 1044 (a pipecolic acid deriv.) in promoting hair growth in mice was shown. A lotion contained 95% ethanol 80.0, a pipecolic acid deriv. 10.0, .alpha.-Tocopherol acetate 0.01, ethylene oxide (40 mol) adducts of

KATHLEEN FULLER EIC1700 308-4290

```
hardened castor oil 0.5, purified water 9.0, perfume and dye q.s. 100%.
ST
     pipecolic acid deriv hair growth promoter
ΙT
     Proteins, specific or class
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (FKBP (FK 506-binding protein); small mol. pipecolic acid deriv. hair
        growth compns. and uses)
IT
     Alopecia
        (areata; small mol. pipecolic acid deriv. hair growth compns. and uses)
ΙŢ
     Drug delivery systems
        (emulsions; small mol. pipecolic acid deriv. hair growth compns. and
        uses)
ΙT
     Hair preparations
        (growth stimulants; small mol. pipecolic acid deriv. hair growth
        compns. and uses)
IT
     Drug delivery systems
        (lotions; small mol. pipecolic acid deriv. hair growth compns. and
        uses)
IT
     Alopecia
        (male pattern; small mol. pipecolic acid deriv. hair growth compns. and
        uses)
     Drug delivery systems
IT
        (ointments, creams; small mol. pipecolic acid deriv. hair growth
        compns. and uses)
TΤ
     Alopecia
     Shampoos
        (small mol. pipecolic acid deriv. hair growth compns. and uses)
TΤ
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (small mol. pipecolic acid deriv. hair growth compns. and uses)
TΤ
     535-75-1D, Pipecolic acid, derivs.
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and uses)
                          186834-77-5, GPI 1102
     104987-11-3, Fk506
                                                   186834-82-2, GPI 1116
IT
                             212607-81-3, GPI 1206
     190444-03-2, GPI 1044
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and
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(77) Zelle; US 5543423 1996 HCAPLUS
     104987-11-3, Fk506 190444-03-2, GPI 1044
IT
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (small mol. pipecolic acid deriv. hair growth compns. and
        uses)
RN
     104987-11-3 HCAPLUS
     15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
CN
     tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
     dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,
                             KATHLEEN FULLER EIC1700 308-4290
```

(3S, 4R, 5S, 8R, 9E, 12S, 14S, 15R, 16S, 18R, 19R, 26aS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 190444-03-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L15

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2001:111510 HCAPLUS
ΑN
     134:168053
DN
     Pipecolic acid derivatives for hair growth compositions and uses
TI
     Steiner, Joseph P.; Hamilton, Gregory S. Gpi Nil Holdings, Inc., USA
IN
PΑ
SO
     U.S., 29 pp.
     CODEN: USXXAM
DT
     Patent
     English
LA
     ICM A61K031-44
IC
     514291000
NCL
     62-3 (Essential Oils and Cosmetics)
CC
     Section cross-reference(s): 1
FAN.CNT 1
                                                APPLICATION NO.
     PATENT NO.
                        KIND
                               DATE
                                                                    DATE
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ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2001 ACS

```
PΙ
     US 6187784
                            20010213
                                            US 1998-89376
                                                             19980603
                       B1
AB
     This invention relates to compns. and methods for treating alopecia and
     promoting hair growth using pipecolic acid derivs. Thus a lotion
     contained a pipecolic acid deriv. 0.05, hinokitiol 0.01, ethoxylated
     castor oil 0.5, water 19.0, perfume and dye qs and EtOH to 80.0%.
ST
     pipecolic acid hair growth; alopecia pipecolic acid hair
     Proteins, specific or class
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (FKBP-12 (FK 506-binding protein, 12,000-mol.-wt.); pipecolic acid
        derivs. for hair growth compns.)
IT
     Hair preparations
        (creams; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (emulsions; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (growth stimulants; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (lotions; pipecolic acid derivs. for hair growth compns.)
IT
     Alopecia
     Shampoos
        (pipecolic acid derivs. for hair growth compns.)
IT
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (pipecolic acid derivs. for hair growth compns.)
ΙT
     53123-88-9, Rapamycin 141084-63-1 147438-30-0
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     RL: BAC (Biological activity or effector, except adverse); BUU (Biological
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        (pipecolic acid derivs. for hair growth compns.)
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RE
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    53123-88-9, Rapamycin 141084-63-1 147438-30-0
    147438-31-1 148493-28-1 149438-31-3, Way
    124466 152754-42-2 153011-31-5, SLB 506
    155255-24-6 155255-27-9 155255-28-0
    155255-29-1 155668-46-5 155668-47-6
    155668-50-1 155668-51-2 156038-45-8
    165047-17-6, Rap Pa 186834-63-9 186834-64-0
    186834-65-1 186834-74-2 186834-75-3
    186834-76-4 186834-83-3 186834-84-4
    186834-85-5 186960-09-8 259225-71-3
    RL: BAC (Biological activity or effector, except adverse); BUU (Biological
    use, unclassified); BIOL (Biological study); USES (Uses)
        (pipecolic acid derivs. for hair growth compns.)
    53123-88-9 HCAPLUS
RN
                     (CA INDEX NAME)
CN
    Rapamycin (9CI)
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Absolute stereochemistry.

Double bond geometry as shown.

PAGE 2-A

Ме

RN 141084-63-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

4 th compound in Claim 20

RN 147438-30-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 147438-31-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 148493-28-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, phenylmethyl ester, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 149438-31-3 HCAPLUS

CN 27,31-Epoxy-5,36-etheno-1H,5H-pyrido[2,1-c][1,2,4]triazolo[1,2-q][1,4,17,18]oxatriazacyclohentriacontine-1,3,9,15,19,25,26(2H,6H,10H,19aH)-heptone, 7,8,11,14,16,17,20,21,22,23,27,28,29,30,31,32,33,36-octadecahydro-11,27-dihydroxy-17-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-10,33-dimethoxy-6,8,12,14,28,34-hexamethyl-2-phenyl-, (6S,8R,10R,11R,12E,14R,17S,19aS,27R,28R,31S,33S,34E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by E or Z. Currently available stereo shown.

PAGE 1-A

PAGE 1-B

RN 152754-42-2 HCAPLUS

CN Pyrido[2,1-c][1,9,4]dioxaazacyclononadecane-1,12,16,17(3H,19H)-tetrone, tetradecahydro-15,15-dimethyl-, (22aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 153011-31-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(1S,2Z)-1-methoxy-2-butenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, (1R,2R,3S)-3-hydroxy-1-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-2-methyl-5-oxo-6-(2-propenyl)-8-nonenyl ester, (2S)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 155255-24-6 HCAPLUS CN 2-Piperidinecarboxyli

2-Piperidinecarboxylic acid, 1-[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 1-methylethyl ester, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 155255-27-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 3-(3,4-dimethoxyphenyl)propyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-B

RN 155255-28-0 HCAPLUS

CN 2-Piperidinecarboxamide, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-N-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 155255-29-1 HCAPLUS

CN 2-Piperidinecarboxamide, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-N-(3-phenylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 155668-46-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(tetrahydro-2-hydroxy-2H-pyran-2-yl)acetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-47-6 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(tetrahydro-2-methoxy-2H-pyran-2-yl)acetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-50-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(3,4-dihydro-2H-pyran-6-yl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-51-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 156038-45-8 HCAPLUS

CN Pyrido[2,1-c][1,9,4]dioxaazacycloheneicosine-1,14,18,19(3H,21H)-tetrone, hexadecahydro-17,17-dimethyl-, (24aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 165047-17-6 HCAPLUS

CN Glycine, (2S)-1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(2S,3S)-3-hydroxy-2-methoxybutyl]-3-methyl-2H-pyran-2-yl]acetyl]-2-piperidinecarbonyl-(.alpha.R)-.alpha.-aminobenzenebutanoylglycyl-N-methyl-, (4.fwdarw.16)-lactone (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-63-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(1-hydroxycyclohexyl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 186834-64-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(1-methoxycyclohexyl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 186834-65-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186834-74-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-75-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 3-phenylpropyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-76-4 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 3-(3-pyridinyl)propyl KATHLEEN FULLER EIC1700 308-4290

ester, (2S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-83-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-84-4 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-cyclohexylpropyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-85-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-phenylpropyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 186960-09-8 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 1-phenylethyl ester, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-B

∠OMe .

RN 259225-71-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, (2Z)-3-phenyl-2-propenyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-B

L15 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:900207 HCAPLUS

DN 134:61215

TI Lipid and detergent-containing topical formulations comprising vesicle delivery systems

IN Niemiec, Susan M.; Nystrand, Glenn A.; Wang, Jonas C. T.; Ho, Kie L.

PA Johnson & Johnson Consumer Products, Inc., USA

SO Eur. Pat. Appl., 41 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K007-00 .

ICS A61K007-06; A61K007-48; A61K009-127

CC 62-1 (Essential Oils and Cosmetics)
 Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	EP 1060732	A2 200012	20 EP 2000-304542	20000526
	R: AT, B	E, CH, DE, DK, E	S, FR, GB, GR, IT, LI, LU	, NL, SE, MC, PT,
	•	I, LT, LV, FI, R	, , , , , , , , , , , , , , , , , , , ,	
	JP 2001019634	A2 200101	23 JP 2000-157251	20000526
	CN 1285186	A 200102	28 CN 2000-117689	20000526
	BR 2000002285	A 200101	23 BR 2000-2285	20000529
PRAI	US 1999-32089	4 A 199905	27	

AB This invention relates to a method for enhancing the transmembrane and/or topical penetration of pharmacol. active substances using a certain vesicle delivery system as an enhancing agent, and an optional detergent, as well as the compns. used therein. Various active agents, such as hair growth agents, hair inhibitor agents, anti-acne agents, depilatory agents, antiaging agents, and depigmentation agents, may be effectively delivered into the skin, hair follicles and sebaceous glands using the compns. of the present invention. For example, liposome delivery systems were prepd. contg. as a lipid phase glyceryl distearate 33.13-40.91, cholesterol

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Cosmetics

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11.04-13.64, polyoxyethylene-10-stearyl ether 29.44-36.36, di(soyoylethyl)
hydroxyethylammonium methosulfate 0-19.03, and elubiol 7.36-9.09 parts,
and as an aq. phase zinc pyrithione 0-8.57, salicylic acid 0-25.07, and
distd. water 74.93-100 parts, resp.
lipid detergent liposome topical; cosmetic hair prepn lipid detergent
liposome
Sulfonic acids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (C14-16-1-alkenesulfonic, sodium salts, Bio-Terge AS 40; topical
   liposomes contg. lipids and detergents for delivery of active agents to
   skin, hair follicles and sebaceous glands)
Heat-shock proteins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (HSP 72; topical liposomes contg. lipids and detergents for delivery of
   active agents to skin, hair follicles and sebaceous glands)
Cosmetics
   (aerosols; topical liposomes contg. lipids and detergents for delivery
   of active agents to skin, hair follicles and sebaceous glands)
Alcohols, biological studies
Amides, biological studies
Fatty acids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (alkoxylated; topical liposomes contg. lipids and detergents for
   delivery of active agents to skin, hair follicles and sebaceous glands)
Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (alkyl group-terminated; topical liposomes contg. lipids and detergents
   for delivery of active agents to skin, hair follicles and sebaceous
   glands)
Phenols, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (alkyl, alkoxylated; topical liposomes contg. lipids and detergents for
   delivery of active agents to skin, hair follicles and sebaceous glands)
Cosmetics
   (antiaging; topical liposomes contg. lipids and detergents for delivery
   of active agents to skin, hair follicles and sebaceous glands)
Hair preparations
   (antidandruff; topical liposomes contg. lipids and detergents for
   delivery of active agents to skin, hair follicles and sebaceous glands)
Lipids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (cationic and nonionic; topical liposomes contq. lipids and detergents
   for delivery of active agents to skin, hair follicles and sebaceous
   glands)
Cosmetics
   (cleansing; topical liposomes contg. lipids and detergents for delivery
   of active agents to skin, hair follicles and sebaceous glands)
Amides, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (coco, N-(hydroxyethyl), Monamid CMA; topical liposomes contg. lipids
   and detergents for delivery of active agents to skin, hair follicles
   and sebaceous glands)
Cosmetics
   (creams; topical liposomes contg. lipids and detergents for delivery of
   active agents to skin, hair follicles and sebaceous glands)
```

(depilatories; topical liposomes contg. lipids and detergents for KATHLEEN FULLER EIC1700 308-4290

delivery of active agents to skin, hair follicles and sebaceous glands) Polysiloxanes, biological studies IT RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (di-Me, 3-hydroxypropyl Me, ethoxylated propoxylated, Abil B 8852; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) Polyoxyalkylenes, biological studies IT RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ethers, with alkyl phenols; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) Fatty acids, biological studies ΙT RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ethoxylated; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) Cosmetics TΤ (gels; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) Hair preparations ΙT (growth inhibitors; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Hair preparations (growth stimulants; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) TΤ Cosmetics Drug delivery systems (liposomes; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) TT (lotions; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) TΤ Cosmetics (mousses; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Drug delivery systems (ointments; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Cosmetics (patches; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Biological transport (permeation, enhancers; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Alcohols, biological studies RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyhydric, esters, ethoxylated; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Protein hydrolyzates RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (silk; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Cosmetics (skin-lightening; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands) IT Cosmetics (sprays; topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands)

```
IT
    Acne
    Bath preparations
     Detergents
     Dissolution rate
     Particle size distribution
     Psoriasis
     Seborrhea
     Shale oils
     Shampoos
     Surfactants
        (topical liposomes contg. lipids and detergents for delivery of active
        agents to skin, hair follicles and sebaceous glands)
IT
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (topical liposomes contg. lipids and detergents for delivery of active
       agents to skin, hair follicles and sebaceous glands)
     Cell adhesion molecules
ΙT
    Coal tar
     Diglycerides
     Interleukin 1.alpha.
     Interleukin 1.beta.
     Interleukin 6
     Keratins
     Sterols
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (topical liposomes contg. Lipids and detergents for delivery of active
       agents to skin, hair follicles and sebaceous glands)
IT
     Drug delivery systems
        (topical; topical liposomes contg. lipids and detergents for delivery
        of active agents to skin, hair follicles and sebaceous glands)
IT
     Drug delivery systems
        (transdermal; topical liposomes contg. lipids and detergents for
        delivery of active agents to skin, hair follicles and sebaceous glands)
IT
     Protein hydrolyzates
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (wheat; topical liposomes contg. lipids and detergents for delivery of
        active agents to skin, hair follicles and sebaceous glands)
IT
     144377-73-1, Phospholipid EFA
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (linoleamidopropyl PG dimonium chloride, Phospholipid EFA; topical
        liposomes contg. lipids and detergents for delivery of active agents to
        skin, hair follicles and sebaceous glands)
ΤТ
     50-23-7, Hydrocortisone
                               50-28-2, 17.beta.-Estradiol, biological studies
                                              56-87-1, L-Lysine, biological
     50-81-7, Vitamin C, biological studies
               57-88-5, Cholesterol, biological studies
                                                          57-92-1,
     Streptomycin, biological studies
                                        58-95-7, Vitamin E acetate
                                                                      59-02-9,
     .alpha.-Tocopherol 66-81-9, Cycloheximide
                                                   68-26-8, Retinol
                                                                       69-72-7,
                                          74-79-3, L-Arginine, biological
     Salicylic acid, biological studies
               77-92-9, Citric acid, biological studies
                                                          81-13-0, Panthenol
     studies
                                  89-78-1, Menthol
                                                      107-41-5, Hexylene glycol
     83-46-5, .beta.-Sitosterol
                                               114-07-8, Erythromycin
     112-80-1, Oleic acid, biological studies
     131-57-7, Oxybenzone
                            139-96-8, TEA lauryl sulfate
                                                            151-21-3, Sodium
     lauryl sulfate, biological studies
                                          152-11-4, Verapamil hydrochloride
                                                  378-44-9, Betamethazone
     302-79-4, Tretinoin
                           364-98-7, Diazoxide
     515-69-5, Bisabolol
                           551-11-1, Prostaglandin F2.alpha.
                                                                637 - 58 - 1,
                               745-65-3, Prostaglandin El
                                                             1314-22-3, Zinc
     Pramoxine hydrochloride
               1323-83-7, Glyceryl distearate
                                                1406-18-4, Vitamin E
     dioxide
                            5466-77-3
                                        7704-34-9, Sulfur, biological studies
     2609-46-3, Amiloride
                                          9005-00-9, Polyoxyethylene stearyl
     9004-82-4, Sodium laureth sulfate
                                         11103-57-4, Vitamin A
                                                                  12001-79-5,
             11096-26-7, Erythropoietin
     ether
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Vitamin K 13463-41-7, Zinc pyrithione 13463-67-7, Titanium dioxide, 13822-09-8, Benzyl peroxide 21829-25-4, Nifedipine biological studies 26590-05-6, Merquat 550 36574-66-0D, N-coco acyl derivs. 38304-91-5, 39236-46-9, Imidazolidinyl urea 42399-41-7, Diltiazem 51234-28-7, Benoxaprofen 56093-45-9, Selenium sulfide 51145-31-4 60559-99-1, N''-Cyano-N-(tert-pentyl)-N-'-3-pyridinyl-guanidine 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 65277-42-1, Ketoconazole 64296-33-9, Vitamin C palmitate 67914-69-6, 81859-24-7, Polyquaternium 10 79217-60-0, Cyclosporin 98113-00-9, Monateric CA 35 94089-18-6, Panthenol triacetate 98319-26-7, Finasteride **104987-11-3**, FK 506 148619-01-6, Plantaren 2000 222171-02-0, Structure Plus-INCI 313227-46-2D, fatty 313352-27-1, Chembetaine CGF 313352-38-4, Tego-Betain E acid derivs. RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands)

IT **104987-11-3**, FK 506

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(topical liposomes contg. lipids and detergents for delivery of active agents to skin, hair follicles and sebaceous glands)

RN 104987-11-3 HCAPLUS

CN

15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

- L15 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2001 ACS
- AN 2000:384175 HCAPLUS
- DN 133:30959
- TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
- IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
- PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
- SO PCT Int. Appl., 166 pp.

CODEN: PIXXD2

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DT
      Patent
LA
      English
      ICM C07D403-04
IC
             CO7D409-12; A61P017-14; A61K031-40; C07D413-04; A61P025-28;
              A61K031-41; C07D207-09; A61P027-00; A61K031-42; C07D403-06;
              A61K031-50; C07D211-34; C07D207-16; C07D405-12
       34-2 (Amino Acids, Peptides, and Proteins)
CC
       Section cross-reference(s): 1
FAN.CNT 1
       PATENT NO.
                              KIND DATE
                                                            APPLICATION NO. DATE
                                       -----
                             A2
      WO 2000032588
                                                            WO 1999-US28663 19991203
                                       20000608
PI
      WO 2000032588
                              A3
                                       20010222
                 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
                  CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
                  AZ, BY, KG, KZ, MD, RU, TJ, TM
            RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-204237
                               Α
                                       19981203
       US 1999-453571
                                Α
                                       19991202
      MARPAT 133:30959
OS
GΙ
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AB Title compds. [I; n = 1-3; X = 0, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

ST prolinylalkanedione prepn neurol disease vision disorder alopecia treatment; memory disorder treatment prolinylalkanedione prepn

IT Nervous system

(Huntington's chorea, treatment; prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

IT Nervous system

(amyotrophic lateral sclerosis, treatment; prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

IT Nervous system

(disease, treatment; prepn. of prolinylalkanediones and related compds. KATHLEEN FULLER EIC1700 308-4290

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for treating neurol. disease, vision disorders, and alopecia)
    Memory, biological
IT
     Vision
        (disorder, treatment; prepn. of prolinylalkanediones and related
        compds. for treating neurol. disease, vision disorders, and alopecia)
     Regeneration, animal
IT
        (nerve, stimulators; prepn. of prolinylalkanediones and related compds.
        for treating neurol. disease, vision disorders, and alopecia)
IT
     Nerve
        (peripheral, damage treatment; prepn. of prolinylalkanediones and
        related compds. for treating neurol. disease, vision disorders, and
        alopecia)
     Anti-Alzheimer's agents
ΙT
     Antiparkinsonian agents
        (prepn. of prolinylalkanediones and related compds. for treating
        neurol. disease, vision disorders, and alopecia)
     Amino acids, preparation
IT
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of prolinylalkanediones and related compds. for treating
        neurol. disease, vision disorders, and alopecia)
IT
     Alopecia
        (treatment; prepn. of prolinylalkanediones and related compds. for
        treating neurol. disease, vision disorders, and alopecia)
IT
     186268-78-0P
                    222171-48-4P
                                    222171-52-0P
                                                   222171-57-5P
                                                                   222171-58-6P
                                                 251949-17-4P
     251917-42-7P
                    251949-15-2P 251949-16-3P
                                                 251949-21-0P
     251949-18-5P
                    251949-19-6P 251949-20-9P
                                  251949-24-3P
                                                 251949-25-4P
     251949-22-1P 251949-23-2P
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                                    251949-28-7P 251949-29-8P
     251949-26-5P
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                                                   251949-87-8P
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                                    251950-01-3P
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                    251950-05-7P
                                    251950-06-8P 251950-07-9P
     251950-04-6P
                                    251950-10-4P
     251950-08-0P
                    251950-09-1P
                                                   251950-11-5P
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     251950-13-7P
                    251950-14-8P
                                    251950-16-0P
                                    251950-21-7P
                                                   251950-22-8P
                                                                   251950-23-9P
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                                    251950-26-2P
                                                   251950-27-3P
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                                    273924-80-4P
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                    273924-79-1P
     273924-78-0P
                                    273924-85-9P
                                                   273924-86-0P
                                                                   273924-87-1P
                    273924-84-8P
     273924-83-7P
     273924-88-2P
                    273924-89-3P
                                    273924-90-6P
                                                   273924-91-7P
                                                                   273924-92-8P
     273924-93-9P
                    273924-94-0P
                                    273925-00-1P
                                                   273925-01-2P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of prolinylalkanediones and related compds. for treating
        neurol. disease, vision disorders, and alopecia)
IT
     79-19-6, Thiosemicarbazide
                                   95-14-7, 1H-Benzotriazole
                                                               100-02-7,
     4-Nitrophenol, reactions
                                 1576-35-8, p-Toluenesulfonylhydrazide
     2133-40-6, L-Proline methyl ester hydrochloride
                                                        2266-41-3
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4755-77-5, Ethyl chlorooxoacetate 5781-53-3, Methyl oxalyl chloride 10393-86-9, Methanesulfonylhydrazide 22059-22-9 7511-13-9 22179-78-8 27469-60-9 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 29335-36-2 32231-06-4 273925-05-6 273925-06-7 RL: RCT (Reactant) (prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia) 207444-86-8P 273925-02-3P 273925-03-4P 273925-04-5P IT 186268-77-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia) IT 251949-16-3P 251949-20-9P 251949-23-2P 251949-26-5P 251949-29-8P 251949-32-3P 251949-44-7P 251949-45-8P 251949-66-3P 251949-78-7P 251949-79-8P 251949-80-1P 251949-81-2P 251950-07-9P RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 251949-16-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethylphenyl)acetyl]- (9CI) (CA INDEX NAME)

RN 251949-20-9 HCAPLUS

2-Piperidinecarboxylic acid, 1-(cyclopentyloxoacetyl)- (9CI) (CA INDEX CN NAME)

251949-23-2 HCAPLUS RN

2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)- (9CI) (CA INDEX CN NAME)

251949-26-5 HCAPLUS RN

2-Piperidinecarboxylic acid, 1-(cycloheptyloxoacetyl)- (9CI) CN NAME)

RN 251949-29-8 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxo-2-thienylacetyl)- (9CI) (CA INDEX NAME)

RN 251949-32-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(2-furanyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-44-7 HCAPLUS

CN 2-Piperidineacetic acid, 1-(2-oxo-2-phenyl-1-thioxoethyl)- (9CI) (CA INDEX NAME)

RN 251949-45-8 HCAPLUS

CN Phosphonic acid, [1-[2-(2-furanyl)-2-oxo-1-thioxoethyl]-2-piperidinyl](9CI) (CA INDEX NAME)

RN 251949-66-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[2-oxo-1-thioxo-2-(3,4,5-trimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)

RN 251949-78-7 HCAPLUS

CN Piperidine, 1-(1H-indol-2-yloxoacetyl)-2-(propylthio)- (9CI) (CA INDEX NAME)

RN 251949-79-8 HCAPLUS

CN Piperidine, 2-(butylthio)-1-(2-furanyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-80-1 HCAPLUS

CN Acetamide, N-[1-(oxo-2-thiazolylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)

RN 251949-81-2 HCAPLUS

CN Propanamide, N-[1-(oxo-2-thienylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)

RN 251950-07-9 HCAPLUS

CN 2-Piperidinepropanoic acid, .beta.,.beta.-dimethyl-1-(2-oxo-2-phenyl-1-thioxoethyl)- (9CI) (CA INDEX NAME)

L15 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:383615 HCAPLUS

DN 133:217476

TI Time-specific occurrence of alopecia in neonatal C57BL mice treated with N-methyl-N-nitrosourea and the therapeutic efficacy of tacrolimus hydrate

AU Yoshizawa, Katsuhiko; Nambu, Hiroyuki; Yamamoto, Daigo; Yang, Jihong; Kiyozuka, Yasuhiko; Shikata, Nobuaki; Tsubura, Airo

CS Department of Pathology II, Kansai Medical University, Osaka, 570-8506, Japan

SO Pathol. Int. (2000), 50(3), 175-184 CODEN; PITEES; ISSN: 1320-5463

PB Blackwell Science Asia Pty Ltd.

DT Journal

LA English

CC 1-7 (Pharmacology)

Alopecia was induced in male and female neonatal C57BL mice by a single i.p. injection of 60 mg/kg N-methyl-N-nitrosourea (MNU). MNU administration was most effective in the 8-day-old mice and less effective in the 5-day-old mice (at active and early anagen stages of the 1st hair cycle, resp.). No alopecia was seen in the day 14 MNU-treated animals (at telogen stage of the 1st hair cycle). MNU effectively induced hair follicular cell apoptosis at the anagen stage by up-regulation of Bax protein without down-modulation of Bcl-2 protein. In day 8 MNU-treated mice, the immunosuppressive agent 0.01% tacrolimus hydrate (FK506), when topically applied for 5 days from 1 day after MNU treatment (before the occurrence of alopecia), decreased the severity of alopecia. However, it did not stimulate hair growth when applied for 5 days from 20 days of age (after occurrence of alopecia).

ST tacrolimus immunosuppressant methylnitroso urea alopecia neonate

IT Proteins, specific or class

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)

(Bax; MNU-induced alopecia in neonatal mice, up-regulation of)

IT Alopecia

Apoptosis

Immunosuppressants

```
Newborn
         (MNU-induced alopecia in neonatal mice, effect of tacrolimus)
     Proteins, specific or class
IT
     RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
     (Occurrence)
         (bcl-2; MNU-induced alopecia in neonatal mice, down-modulation of)
ΙT
         (follicle; MNU-induced alopecia in neonatal mice, effect of tacrolimus)
ΙT
     Drug delivery systems
         (topical; MNU-induced alopecia in neonatal mice, effect of tacrolimus)
IT
     684-93-5, MNU
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
         (MNU-induced alopecia in neonatal mice, effect of tacrolimus)
     104987-11-3, FK506 109581-93-3, Tacrolimus hydrate
IT
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
         (MNU-induced alopecia in neonatal mice, effect of tacrolimus)
RE.CNT
RE
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     104987-11-3, FK506 109581-93-3, Tacrolimus hydrate
ΙT
     RL: BAC (Biological activity or effector, except adverse); THU
      (Therapeutic use); BIOL (Biological study); USES (Uses)
         (MNU-induced alopecia in neonatal mice, effect of tacrolimus)
RN
     104987-11-3 HCAPLUS
     15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
CN
     tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
     dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,
      (3S, 4R, 5S, 8R, 9E, 12S, 14S, 15R, 16S, 18R, 19R, 26aS) - (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.
Double bond geometry as shown.

RN 109581-93-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,monohydrate, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.

PAGE 1-A

PAGE 1-B

0

● н20

PAGE 2-B

```
H<sub>2</sub>C Me Me
```

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ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2001 ACS
L15
     2000:368433 HCAPLUS
ΑN
DN
     133:831
ΤI
     Regulation of hair follicle morphogenesis based on .beta.-catenin
ΙN
     Gat, Uri; Dasgupta, Ramanuj; Degenstein, Linda; Fuchs, Elaine
PΑ
     Arch Development Corp., USA
SO
     PCT Int. Appl., 127 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
     C07K014-47; A61P017-14
IC
CC
     1-12 (Pharmacology)
     Section cross-reference(s): 3, 13
FAN.CNT 1
     PATENT NO.
                        KIND
                              DATE
                                               APPLICATION NO.
                                                                 DATE
                              20000602
                                              WO 1999-US27490
     WO 2000031134
                        A1
                                                                 19991119
PΙ
             AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
              CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
              IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-109284
                              19981120
                        Ρ
     The present invention provides a method for inducing hair growth by
AΒ
     providing .beta.-catenin activity to a skin cell. This may be achieved by
     providing a .beta.-catenin polypeptide, providing a .beta.-catenin
     agonist, providing a polynucleotide encoding a .beta.-catenin polypeptide,
     enhancing the de novo synthesis of .beta.-catenin, increasing the
     stability or decreasing the degrdn. of .beta.-catenin polypeptides.
     Specifically, a tissue-specific K14 promoter is used to drive the
     expression of an N-terminally truncated human .beta.-catenin mutant
     (.DELTA.N87.beta.cat) in skin. The results indicate that .beta.-catenin
     is a key factor in controlling hair follicle morphogenesis. The
     expression of .DELTA.N87.beta.cat in the basal layer of the epidermis and
     follicle outer root sheath reprograms these cells to induce hair follicle
     morphogenesis. The inventors show that the process of hair follicle
     morphogenesis occurs, including the development of dermal papilla and
     cebaceous glands normally established only in embryogenesis, and hair
     shaft prodn. typical of both initial and cycling follicles. As de novo
     induction of hair follicles will result in the growth of new hairs, the
     invention will be useful therapy for hair growth and alopecia disorders in
     humans and the induction of hair growth in sheep and other livestock.
     hair follicle morphogenesis catenin; gene therapy alopecia catenin
ST
IT
     Transcription factors
```

```
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (Lef-1, activation during hair follicle morphogenesis; regulation of
        hair follicle morphogenesis based on .beta.-catenin)
     Susceptibility (genetic)
IT
        (estg. propensity for alopecia by evaluation of .beta.-catenin
        expression; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
IT
     Hair
        (follicle; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
ΙT
     Skin
        (gene therapy for; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
IT
     Promoter (genetic element)
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immediate early, .beta.-catenin gene therapy driven by; regulation of
        hair follicle morphogenesis based on .beta.-catenin)
     Proteins, specific or class
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (involucrins, .beta.-catenin gene therapy driven by promoter for;
        regulation of hair follicle morphogenesis based on .beta.-catenin)
IT
     Skin
        (keratinocyte, gene therapy for; regulation of hair follicle
       morphogenesis based on .beta.-catenin)
IT
     Drug delivery systems
        (liposomes; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
IT
     Proteins, specific or class
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (loricrins, .beta.-catenin gene therapy driven by promoter for;
        regulation of hair follicle morphogenesis based on .beta.-catenin)
    Gene therapy
IT
    Morphogenesis, animal
        (regulation of hair follicle morphogenesis based on .beta.-catenin)
IT
    Transplant and Transplantation
        (skin; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
IT
     Hedgehog protein
    RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (sonic, apolarized expression in .beta.-catenin transgenic mice;
        regulation of hair follicle morphogenesis based on .beta.-catenin)
IT
     Skin
        (transplant; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
ΙT
    Actins
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (.beta.-, .beta.-catenin gene therapy driven by promoter for;
       regulation of hair follicle morphogenesis based on .beta.-catenin)
IT
    Catenins
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (.beta.-; regulation of hair follicle morphogenesis based on
        .beta.-catenin)
IT
    Filaggrin
    Keratins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (.beta.-catenin gene therapy driven by promoter for; regulation of hair
        follicle morphogenesis based on .beta.-catenin)
IT
    Cytomegalovirus
     Rous sarcoma virus
     Simian virus 40
        (.beta.-catenin gene therapy driven by promoter from; regulation of
       hair follicle morphogenesis based on .beta.-catenin)
ΙT
     Ecdysteroids
```

```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (.beta.-catenin gene therapy driven by promoter regulated by;
        regulation of hair follicle morphogenesis based on .beta.-catenin)
     Adeno-associated virus
TT
     Adenoviridae
     Alopecia
     Polyomavirus
     Vaccinia virus
        (.beta.-catenin gene therapy driven by viral vectors; regulation of
        hair follicle morphogenesis based on .beta.-catenin)
     Retroviral vectors
IT
     Virus vectors
        (.beta.-catenin gene therapy driven by; regulation of hair follicle
        morphogenesis based on .beta.-catenin)
IT
     Promoter (genetic element)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (.beta.-catenin gene therapy driven by; regulation of hair follicle
        morphogenesis based on .beta.-catenin)
ΙT
     79217-60-0, Cyclosporin 104987-11-3, FK506
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (synchronous hair cycle initiated by; regulation of
      hair follicle morphogenesis based on .beta.-catenin)
     60-54-8, Tetracycline
ΤТ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (.beta.-catenin gene therapy driven by promoter regulated by;
        regulation of hair follicle morphogenesis based on .beta.-catenin)
RE.CNT
RE
(1) Behrens, J; NATURE 1996, V382, P638 HCAPLUS
(2) Gat, U; CELL 1998, V95, P605 HCAPLUS
(3) Max-DelbrUck-Centrum FUr Molekulare Medizin; WO 9942481 A 1999 HCAPLUS
(4) Molenaar, M; CELL 1996, V86, P391 HCAPLUS
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(7) The Regents Of The University Of California; WO 9717982 A 1997 HCAPLUS
IT
     104987-11-3, FK506
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (synchronous hair cycle initiated by; regulation of
      hair follicle morphogenesis based on .beta.-catenin)
     104987-11-3 HCAPLUS
RN
     15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
CN
     tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
     dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,
     (3S, 4R, 5S, 8R, 9E, 12S, 14S, 15R, 16S, 18R, 19R, 26aS) - (9CI) (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

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ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2001 ACS
L15
ΑN
     2000:227463 HCAPLUS
DN
     132:269827
ΤI
     Method of treating hair loss using ketoamides
     Tiesman, Jay Patrick; Fulmer, Andrew Wayne; McIver, John Mcmillan;
IN
     Degenhardt, Charles Raymond; Eickhoff, David Joseph
PA
     The Procter & Gamble Company, USA
SO
     PCT Int. Appl., 71 pp.
     CODEN: PIXXD2
DΤ
     Patent
LA
     English
     ICM A61K007-00
IC
CC
     62-3 (Essential Oils and Cosmetics)
     Section cross-reference(s): 27, 63
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO.
                             20000406
PΙ
     WO 2000018358
                       Α2
                                            WO 1999-US22215
                                                             19990924
     WO 2000018358
                       A3
                            20000727
         W: AU, BR, CA, CN, JP, MX
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     AU 6060299
                                            AU 1999-60602
                            20000417
                                                             19990924
                       Α1
                            19980930
PRAI US 1998-102458
                       Ρ
                       W
                            19990924
     WO 1999-US22215
AB
     The present disclosure describes methods for treating hair loss in
     mammals, including arresting and/or reversing hair loss and promoting hair
     growth. The methods comprise administering a pyrrolidinyl or piperidinyl
     ketoamide and a pharmaceutically-acceptable carrier. (S)-N-(3,4,5-
     trimethoxyphenylglyoxyl)pipecolic acid 1,7-diphenyl-4-heptylamide was
     prepd. and incorporated into a topical compn.
ST
     hair loss keto amide
     Hair preparations
IT
        (growth stimulants; treating hair loss using ketoamides)
     Drug delivery systems
IT
        (oral; treating hair loss using ketoamides)
     Amides, biological studies
ΙŢ
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (oxo; treating hair loss using ketoamides)
                             KATHLEEN FULLER EIC1700 308-4290
```

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IT
    Drug delivery systems
        (topical; treating hair loss using ketoamides)
IT
    Alopecia
        (treating hair loss using ketoamides)
     145912-40-9P 186268-54-2P
                                  186268-71-3P 188614-93-9P
IT
     263239-96-9P 263239-97-0P
     RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (treating hair loss using ketoamides)
                                         2046-18-6, 4-Phenylbutyronitrile
TΤ
     637-59-2, 1-Bromo-3-phenylpropane
                  88755-16-2, 3,4,5-Trimethoxyphenylglyoxylic acid
     26250-84-0
    262608-73-1
    RL: RCT (Reactant)
        (treating hair loss using ketoamides)
TΤ
     262608-86-6P
                    263238-16-0P
                                  263238-17-1P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (treating hair loss using ketoamides)
     145912-40-9P 188614-93-9P 263239-96-9P
IT
    263239-97-0P
    RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (treating hair loss using ketoamides)
RN
     145912-40-9 HCAPLUS
CN
     2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-,
     4-phenyl-1-(3-phenylpropyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 188614-93-9 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-,
4-phenyl-1-[2-(3-pyridinyl)ethyl]butyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 263239-96-9 HCAPLUS

CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[4-phenyl-1-(3-phenylpropyl)butyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} \text{Ph} & \text{(CH2)} \text{ 3} \\ \text{HN} & \text{O} \\ \text{S} & \text{N} \\ \text{O} \end{array} \begin{array}{c} \text{OMe} \\ \text{OMe} \\ \text{OMe} \\ \text{OMe} \\ \end{array}$$

RN 263239-97-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 1-(4-phenoxyphenyl)-4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L15 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:784078 HCAPLUS

DN 132:22860

TI Preparation of aza-heterocyclic compounds used to treat neurological KATHLEEN FULLER EIC1700 308-4290

```
disorders and hair loss
     Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
IN
     Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
PΑ
     PCT Int. Appl., 96 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
     ICM C07D207-16
IC
     ICS A61K031-40; C07D207-12; C07D403-04; A61K031-41
     27-1 (Heterocyclic Compounds (One Hetero Atom))
CC
     Section cross-reference(s): 1, 34
FAN.CNT 3
                                             APPLICATION NO.
     PATENT NO.
                       KIND DATE
                                                              DATE
                             -----
     ------
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     WO 9962881
                             19991209
                                             WO 1998-US25573 19981203
                       A1
PΙ
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
             MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9917081
                        A1
                             19991220
                                             AU 1999-17081
                                                               19981203
                                             BR 1998-15920
                                                               19981203
     BR 9815920
                        Α
                             20010220
     EP 1084107
                        A1
                             20010321
                                             EP 1998-961866
                                                               19981203
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                             20010202
                                             NO 2000-5903
                                                               20001121
     NO 2000005903
                        Α
                        P
                             19980603
PRAI US 1998-87788
     US 1998-101077
                        Р
                             19980918
     WO 1998-US25573
                        W
                             19981203
     MARPAT 132:22860
OS
GΙ
```

$$\begin{array}{c|c}
 & (CH_2)_n \\
 & DR^2 \\
 & C(X)C(0)R^1 & I
\end{array}$$

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = 0, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

ST aza heterocyclic prepn neurol disorder hair loss treatment; neurol disorder disorder aza heterocyclic; hair loss disorder aza heterocyclic; heterocyclic carboxylic acid prepn neurol disorder hair loss treatment IT Nervous system

(disease; prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

IT Alopecia

(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

IT 186268-78-0P 222171-48-4P 222171-57-5P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
KATHLEEN FULLER EIC1700 308-4290

```
SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of aza-heterocyclic compds. used to treat neurol. disorders and
        hair loss)
                    222171-58-6P
                                    251917-42-7P
                                                   251949-15-2P
IT
     222171-52-0P
                    251949-17-4P
                                                   251949-19-6P
     251949-16-3P
                                    251949-18-5P
     251949-20-9P
                    251949-21-0P
                                    251949-22-1P 251949-23-2P
                                                 251949-27-6P
     251949-24-3P
                    251949-25-4P 251949-26-5P
     251949-28-7P 251949-29-8P
                                  251949-30-1P
                                                 251949-31-2P
                                                   251949-35-6P
     251949-32-3P
                    251949-33-4P
                                    251949-34-5P
                                                                   251949-40-3P
     251949-36-7P
                    251949-37-8P
                                    251949-38-9P
                                                   251949-39-0P
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                    251949-42-5P
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     251949-52-7P
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                                   251949-55-0P
                                                   251949-56-1P
                                    251949-60-7P
     251949-58-3P
                    251949-59-4P
                                                   251949-61-8P
                                                                  251949-62-9P
                                    251949-65-2P 251949-66-3P
     251949-63-0P
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                                                   251949-70-9P
     251949-67-4P
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                                    251949-69-6P
                                                                   251949-71-0P
                                   251949-74-3P
                                                   251949-75-4P
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                    251949-73-2P
     251949-72-1P
     251949-77-6P 251949-78-7P 251949-79-8P
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     251949-80-1P 251949-81-2P
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     251949-84-5P
                    251949-85-6P
                                    251949-86-7P
                                                   251949-87-8P
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     251949-89-0P
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     251949-99-2P
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                                                   251950-11-5P
     251950-08-0P
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     251950-28-4P
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     251950-33-1P
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                                                   251950-36-4P
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     251950-38-6P
                    251950-39-7P
                                    251950-40-0P
                                                   251950-41-1P
                                                                   251950-42-2P
     251950-43-3P
    RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
    preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of aza-heterocyclic compds. used to treat neurol. disorders and
     hair loss)
ΙT
     543-27-1, Isobutyl chloroformate
                                         2133-40-6, L-Proline methyl ester
    hydrochloride
     RL: RCT (Reactant)
        (prepn. of aza-heterocyclic compds. used to treat neurol. disorders and
        hair loss)
IT
     186268-77-9P
                    207444-86-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of aza-heterocyclic compds. used to treat neurol. disorders and
        hair loss)
RE.CNT
        7
RE
(1) Ariad Gene Therapeutics Inc; WO 9606097 A 1996 HCAPLUS
(2) Ariad Gene Therapeutics Inc; WO 9731898 A 1997 HCAPLUS
(3) Guilford Pharm Inc; WO 9640633 A 1996 HCAPLUS
(4) Guilford Pharm Inc; WO 9837885 A 1998 HCAPLUS
(5) Guilford Pharm Inc; WO 9855090 A 1998 HCAPLUS
(6) Guilford Pharm Inc; WO 9855091 A 1998 HCAPLUS
(7) Pharma, V; WO 9200278 A 1992 HCAPLUS
     251949-16-3P 251949-20-9P 251949-23-2P
IT
     251949-26-5P 251949-29-8P 251949-32-3P
     251949-44-7P 251949-45-8P 251949-50-5P
     251949-51-6P 251949-52-7P 251949-66-3P
     251949-78-7P 251949-79-8P 251949-80-1P
     251949-81-2P 251950-07-9P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
```

preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 251949-16-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethylphenyl)acetyl]- (9CI) (CA INDEX NAME)

RN 251949-20-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclopentyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-23-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-26-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cycloheptyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-29-8 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxo-2-thienylacetyl)- (9CI) (CA INDEX NAME)

RN 251949-32-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(2-furanyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-44-7 HCAPLUS

CN 2-Piperidineacetic acid, 1-(2-oxo-2-phenyl-1-thioxoethyl)- (9CI) (CA INDEX NAME)

RN 251949-45-8 HCAPLUS

CN Phosphonic acid, [1-[2-(2-furanyl)-2-oxo-1-thioxoethyl]-2-piperidinyl]- (9CI) (CA INDEX NAME)

RN 251949-50-5 HCAPLUS

CN 2-Piperidineheptanoic acid, 1-(oxophenylacetyl)- (9CI) (CA INDEX NAME)

RN 251949-51-6 HCAPLUS

CN 2-Piperidineacetic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]- (9CI) (CA KATHLEEN FULLER EIC1700 308-4290

INDEX NAME)

RN 251949-52-7 HCAPLUS

CN Piperidine, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-2-(1H-tetrazol-5-ylmethyl)- (9CI) (CA INDEX NAME)

RN 251949-66-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[2-oxo-1-thioxo-2-(3,4,5-trimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)

RN 251949-78-7 HCAPLUS

CN Piperidine, 1-(1H-indol-2-yloxoacetyl)-2-(propylthio)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
H & O & O \\
N & \parallel & \parallel \\
C - C - N \\
\end{array}$$
n-Prs

RN 251949-79-8 HCAPLUS

CN Piperidine, 2-(butylthio)-1-(2-furanyloxoacetyl)- (9CI) (CA INDEX NAME)

RN 251949-80-1 HCAPLUS

CN Acetamide, N-[1-(oxo-2-thiazolylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)

RN 251949-81-2 HCAPLUS

CN Propanamide, N-[1-(oxo-2-thienylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)

RN 251950-07-9 HCAPLUS

CN 2-Piperidinepropanoic acid, .beta.,.beta.-dimethyl-1-(2-oxo-2-phenyl-1-thioxoethyl)- (9CI) (CA INDEX NAME)

L15 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:783911 HCAPLUS

DN 132:26640

TI Small molecule pipecolic acid derivative hair growth compositions and uses

IN Hamilton, Gregory S.; Steiner, Joseph P.

PA Guilford Pharmaceuticals Inc., USA

SO PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K007-48

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ICS A61K031-445
CC
     62-3 (Essential Oils and Cosmetics)
FAN.CNT 1
                                           APPLICATION NO.
                                                           DATE
     PATENT NO.
                     KIND DATE
                                           -----
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                      _---
                            -----
                     A1
                           19991209
                                          WO 1998-US11264 19980603
    WO 9962491
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        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
                                           AU 1998-77176
                                                            19980603
                           19991220
     AU 9877176
                      A1
                            20010321
                                          EP 1998-925163
                                                           19980603
     EP 1083874
                       Α1
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                            19980603
PRAI WO 1998-US11264
                      Α
    MARPAT 132:26640
OS
     This invention relates to topical compns. and methods for treating
AΒ
     alopecia and promoting hair growth using pipecolic acid derivs. For
     example, 4-phenyl-1-(3-phenylpropyl)butyl 1-(3,3-dimethyl-2-oxopentanoyl)-
     2-piperidinecarboxylate and 1-phenethyl-3-phenylpropyl-1-(3,3-dimethyl-2-
     oxopentanoyl)-2-piperidinecarboxylate showed hair revitalizing properties
     in C57 black mice.
ST
    piperidinecarboxylate deriv alopecia treatment; hair growth promoter
    pipecolate deriv
     Immunophilins
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (affinity to; pipecolic acid derivs. for hair growth compns.)
TT
    Hair preparations
        (creams; pipecolic acid derivs. for hair growth compns.)
     Hair preparations
IT
        (emulsions; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (growth stimulants; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (lotions; pipecolic acid derivs. for hair growth compns.)
IT
     Alopecia
     Shampoos
        (pipecolic acid derivs. for hair growth compns.)
                             141084-12-0 141084-13-1
ΙT
     141083-86-5 141084-02-8
     141084-14-2 141084-34-6 141084-35-7
     141084-39-1 141084-41-5 141084-42-6
                   141097-91-8
                                 186834-77-5
                                              186834-82-2
     141084-63-1
     188614-85-9 188614-86-0 190444-03-2, GPI 1044
     RL: BAC (Biological activity or effector, except adverse); BUU (Biological
     use, unclassified); BIOL (Biological study); USES (Uses)
        (pipecolic acid derivs. for hair growth compns.)
RE.CNT
RE
(1) Fujisawa Pharm Co, Ltd; EP 0423714 A 1991 HCAPLUS
(2) Guilford Pharm Inc; WO 9813343 A 1998 HCAPLUS
ΙT
     141083-86-5 141084-02-8 141084-34-6
     141084-35-7 141084-39-1 141084-41-5
     141084-42-6 141084-63-1 188614-85-9
     188614-86-0 190444-03-2, GPI 1044
     RL: BAC (Biological activity or effector, except adverse); BUU (Biological
     use, unclassified); BIOL (Biological study); USES (Uses)
        (pipecolic acid derivs. for hair growth compns.)
     141083-86-5 HCAPLUS
RN
     2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, phenylmethyl ester,
CN
                 (CA INDEX NAME)
     (2S) - (9CI)
                             KATHLEEN FULLER EIC1700 308-4290
```

Absolute stereochemistry.

RN 141084-02-8 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(2-furanyloxoacetyl)-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141084-34-6 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-cyclohexylbutyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141084-35-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-cyclohexylbutyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 141084-39-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, (3-phenoxyphenyl)methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141084-41-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141084-42-6 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 141084-63-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 188614-85-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 2-phenylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 188614-86-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 3-(1H-indol-3-yl)propyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 190444-03-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

```
ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2001 ACS
L15
     1999:783908 HCAPLUS
AN
     132:26637
DN
ΤI
     Heterocyclic thioester and ketone hair growth compositions and uses
     Hamilton, Gregory S.; Steiner, Joseph P.
IN
PA
     Guilford Pharmaceuticals Inc., USA
SO
     PCT Int. Appl., 102 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM
          A61K007-48
          A61K031-40; A61K031-44; A61K031-445; A61K031-425; A61K031-415;
          A61K031-535; A61K031-54
CC
     62-3 (Essential Oils and Cosmetics)
     Section cross-reference(s): 28
FAN.CNT 1
     PATENT NO.
                      KIND
                             DATE
                                            APPLICATION NO.
                                                              DATE
                             19991209
                                            WO 1998-US11251
                                                              19980603
ΡI
     WO 9962488
                       A1
             AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
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KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, KATHLEEN FULLER EIC1700 308-4290

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CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9877171
                       Α1
                            19991220
                                            AU 1998-77171
                                                             19980603
     EP 1083873
                       A1
                            20010321
                                            EP 1998-925157
                                                             19980603
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
             IE, SI, LT, LV, FI, RO
PRAI WO 1998-US11251
                            19980603
                       Α
OS
     MARPAT 132:26637
     This invention relates to pharmaceutical compns. and methods for treating
AΒ
     alopecia and promoting hair growth using heterocyclic thioesters and
               Thus, 2-phenyl-1-ethyl-(2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-
     pyrrolidinecarbothicate (I) was prepd. by the reaction of Me
     pipecolate-HCl with Me oxalyl chloride followed by the reaction with
     1,1-dimethylpropylmagnesium chloride, hydrolysis and reaction with Ph
     mercaptan. A hair lotion contained 95% EtOh 80.0, I 0.005, hinokitol
     0.01, ethoxylated hardened castor oil 0.5, and water 19.0%, and perfume
     and dye qs.
     thioester heterocyclic hair growth prepn; ketones heterocyclic hair growth
ST
     prepn
IT
     Hair preparations
        (creams; heterocyclic thioesters and ketones for hair growth compns.)
TΤ
     Hair preparations
        (emulsions; heterocyclic thioesters and ketones for hair growth
        compns.)
TT
     Hair preparations
        (growth stimulants; heterocyclic thioesters and ketones for hair growth
        compns.)
ΤТ
     Alopecia
     Shampoos
        (heterocyclic thioesters and ketones for hair growth compns.)
     Immunophilins
TΤ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (heterocyclic thioesters and ketones for hair growth compns.)
     Ketones, biological studies
IT
     RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (heterocyclic; heterocyclic thioesters and ketones for hair growth
        compns.)
ΙT
     Hair preparations
        (lotions; heterocyclic thioesters and ketones for hair growth compns.)
ΙT
     Carboxylic acids, biological studies
     RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (thiocarboxylic, esters, heterocyclic; heterocyclic thioesters and
        ketones for hair growth compns.)
IT
     205388-13-2P
                    205388-14-3P
                                    205388-15-4P
                                                   205388-16-5P
                                                                   205388-17-6P
     205388-18-7P
                    205388-19-8P
                                    205388-20-1P
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     205388-24-5P
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                    205388-55-2P
                                    205388-60-9P
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     205388-80-3P
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     217180-90-0P
                    251948-44-4P
                                                   251948-46-6P
     251948-47-7P
                    251948-48-8P
     RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (heterocyclic thioesters and ketones for hair growth compns.)
IT
                                             955-40-8
                                                                     4830-93-7
     108-98-5, Phenylmercaptan, reactions
                                                        2133-40-6
                                         28276-08-6
                                                      32559-18-5
                                                                    139419-63-9
     5781-53-3, Methyloxalyl chloride
```

186268-77-9

RL: RCT (Reactant)

(heterocyclic thioesters and ketones for hair growth compns.)

IT 186268-78-0P 205388-64-3P 205388-65-4P 205388-66-5P 205388-67-6P

205388-68-7P 222171-23-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(heterocyclic thioesters and ketones for hair growth compns.)

RE.CNT 4

RE

- (1) Fujisawa Pharm Co Ltd; EP 0423714 A 1991 HCAPLUS
- (2) Guilford Pharm Inc; WO 9813343 A 1998 HCAPLUS
- (3) Hallam, K; EP 0471135 A 1992 HCAPLUS
- (4) Merck & Co Inc; WO 9314762 A 1993 HCAPLUS
- IT 205388-48-3P 205388-54-1P 217179-50-5P

217180-90-0P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heterocyclic thioesters and ketones for hair growth compns.)

RN 205388-48-3 HCAPLUS

CN 2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-(2-phenylethyl) ester (9CI) (CA INDEX NAME)

RN 205388-54-1 HCAPLUS

CN 2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-[3-(4-methoxyphenyl)propyl] ester (9CI) (CA INDEX NAME)

MeO 
$$\begin{array}{c|c} O & O \\ | & O \\ | & O \\ Ph-C-C \\ | & | \\ O & O \\ \end{array}$$

RN 217179-50-5 HCAPLUS

CN 2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-[3-phenyl-1-(2-phenylethyl)propyl] ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & O \\
\parallel & \parallel \\
C - C - Ph
\end{array}$$

$$\begin{array}{c|c}
C - S - CH - CH_2 - CH_2 - Ph \\
\parallel & \mid \\
O & CH_2 - CH_2 - Ph
\end{array}$$

RN 217180-90-0 HCAPLUS

CN Piperidine, 1-(cyclohexyloxoacetyl)-2-(1-oxo-6-phenylhexyl)- (9CI) (CA INDEX NAME)

ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2001 ACS

L15

```
1999:783903 HCAPLUS
ΑN
DN
     132:26633
     Pipecolic acid derivatives for hair growth compositions
ΤI
     Hamilton, Gregory S.; Steiner, Joseph P.
IN
     Guilford Pharmaceuticals, Inc., USA
PA
     PCT Int. Appl., 103 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K007-48
         A61K031-50; A61K031-435; A61K031-445; C07K005-02; C07K005-08
     62-3 (Essential Oils and Cosmetics)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
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                      ____
PΙ
     WO 9962483
                       A1
                            19991209
                                           WO 1998-US11242 19980603
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             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9877167
                            19991220
                                           AU 1998-77167
                                                            19980603
                       Α1
     EP 1083872
                       A1
                            20010321
                                           EP 1998-925152
                                                            19980603
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRAI WO 1998-US11242
                           19980603
                      Α
     This invention relates to pharmaceutical compns. and methods for treating
AB
     alopecia and promoting hair growth using pipecolic acid derivs.
     hair lotion contained 95% EtOH, a pipecolic acid deriv. such as
     4-(4-methoxyphenyl)butyl 1-(2-oxo-2-phenylacetyl)-2-piperidinecarboxylate
     10.0, .alpha.-tocopherol acetate 0.01, ethoxylateed hardened castor oil
                             KATHLEEN FULLER EIC1700 308-4290
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```
0.5, and water 9.0%, and perfume and dye.
ST
     pipecolic acid deriv hair growth
IT
     Hair preparations
        (creams; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (emulsions; pipecolic acid derivs. for hair growth compns.)
     Hair preparations
IT
        (growth stimulants; pipecolic acid derivs. for hair growth compns.)
IT
     Hair preparations
        (lotions; pipecolic acid derivs. for hair growth compns.)
IT
     Alopecia
     Immunosuppressants
     Shampoos
        (pipecolic acid derivs. for hair growth compns.)
IT
     Immunophilins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (pipecolic acid derivs. for hair growth compns.)
     535-75-1D, Pipecolic acid, derivs. 53123-88-9, Rapamycin
IT
     141084-63-1 145021-24-5
                               145021-25-6
                                              145021-36-9
                   145021-38-1
                                  145021-39-2
                                                145021-43-8
                                                              145021-46-1
     145021-37-0
     145021-47-2
                   145037-51-0 147438-29-7 149438-31-3, Way
                                                         152754-37-5
              152754-34-2
                            152754-35-3
                                           152754-36-4
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                   152754-39-7
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     152754-38-6
     153011-31-5, SBL 506 155255-30-4 155255-31-5
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     155255-32-6 155367-80-9
                               155399-01-2
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     155668-54-5
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     252002-79-2 252002-81-6 252002-83-8
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     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (pipecolic acid derivs. for hair growth compns.)
RE.CNT
RE
(1) Armistead, D; US 5620971 A 1997 HCAPLUS
(2) Astra Aktiebolaget; WO 9611943 A 1996 HCAPLUS
(3) Fujisawa Pharm Co Ltd; EP 0423714 A 1987 HCAPLUS
(4) Guilford Pharm; WO 9813343 A 1998 HCAPLUS
(5) Nelson, F; US 5385908 A 1995 HCAPLUS
(6) Skotnicki, J; US 5252579 A 1993 HCAPLUS
     53123-88-9, Rapamycin 141084-63-1 145021-24-5
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     252002-83-8 252002-96-3
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RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pipecolic acid derivs. for hair growth compns.)

RN 53123-88-9 HCAPLUS

CN Rapamycin (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 2-A

PAGE 1-A

Ме

RN 141084-63-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 145021-24-5 HCAPLUS

CN L-Phenylalanine, N-[[(2S)-1-[[5-[(1E,3R)-4-hydroxy-3-methyl-1-butenyl]-2-KATHLEEN FULLER EIC1700 308-4290

thienyl]oxoacetyl]-2-piperidinyl]carbonyl]-, 1,1-dimethylethyl ester (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 147438-29-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, (1S,4R,5E)-1-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-4,6-dimethyl-3,7-dioxo-5-heptenyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-B

RN 149438-31-3 HCAPLUS

CN 27,31-Epoxy-5,36-etheno-1H,5H-pyrido[2,1-c][1,2,4]triazolo[1,2-q][1,4,17,18]oxatriazacyclohentriacontine-1,3,9,15,19,25,26(2H,6H,10H,19aH)-heptone, 7,8,11,14,16,17,20,21,22,23,27,28,29,30,31,32,33,36-KATHLEEN FULLER EIC1700 308-4290

octadecahydro-11,27-dihydroxy-17-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-10,33-dimethoxy-6,8,12,14,28,34-hexamethyl-2-phenyl-, (6S,8R,10R,11R,12E,14R,17S,19aS,27R,28R,31S,33S,34E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.

Currently available stereo shown.

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 152754-42-2 HCAPLUS

CN Pyrido[2,1-c][1,9,4]dioxaazacyclononadecane-1,12,16,17(3H,19H)-tetrone, tetradecahydro-15,15-dimethyl-, (22aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 153011-31-5 HCAPLUS .

CN 2-Piperidinecarboxylic acid, 1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(1S,2Z)-1-methoxy-2-butenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, (1R,2R,3S)-3-hydroxy-1-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-2-methyl-5-oxo-6-(2-propenyl)-8-nonenyl ester, (2S)- (9CI) (CA INDEX NAME)

PAGE 1-A

$$Me-CH=CH-CH$$

$$Me-CH=CH-CH$$

$$Me$$

$$C=0$$

$$C=0$$

$$C=0$$

$$H_2C=CH-CH_2-CH-CH-CH-CH-CH-O-C$$

$$H_2C=CH-CH_2$$

$$Me-CH$$

$$CH_2$$

$$OMe$$

$$OMe$$

PAGE 2-A

RN 155255-30-4 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(2S,3E,5E,7E,9S,11R,13R,14R,15E,17R,19E,21R)-14-hydroxy-22-[(1S,3R,4R)-4hydroxy-3-methoxycyclohexyl]-2,13-dimethoxy-3,9,11,15,17,21-hexamethyl-12,18-dioxo-3,5,7,15,19-docosapentaenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-B

PAGE 1-A

RN 155255-31-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo[(2R,3R,6S)-tetrahydro-2-hydroxy-6-[(2S,3E,5E,7E,9S,11R,13R,14R,15E,17R,19E,21R)-14-hydroxy-22-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-2,13-dimethoxy-3,9,11,15,17,21-hexamethyl-12,18-dioxo-3,5,7,15,19-docosapentaenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-B

RN 155367-80-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(4,5-dideoxy-4-methyl-6,8-di-0-methyl-.alpha.-D-ribo-2,3-octodiulo-3,7-pyranosonoyl)-, (1S)-1-[(1E)-2-[(3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-5-hexenyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

$$H_2C$$
 (CH<sub>2</sub>)<sub>3</sub> O OH OH R R S OME OME

RN 155668-46-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(tetrahydro-2-hydroxy-2H-pyran-2-yl)acetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-47-6 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[oxo(tetrahydro-2-methoxy-2H-pyran-2-yl)acetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-50-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(3,4-dihydro-2H-pyran-6-yl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 155668-51-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 156038-45-8 HCAPLUS

CN Pyrido[2,1-c][1,9,4]dioxaazacycloheneicosine-1,14,18,19(3H,21H)-tetrone, hexadecahydro-17,17-dimethyl-, (24aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186834-63-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(1-hydroxycyclohexyl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 186834-64-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(1-methoxycyclohexyl)oxoacetyl]-, ethyl ester (9CI) (CA INDEX NAME)

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RN 186834-65-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186959-50-2 HCAPLUS

CN Pyrido[2,1-c][1,11,4]dioxaazacycloheneicosine-1,7,14,18,19(8H,15H,21H)-pentone, 3,4,5,6,11,12,16,17,22,23,24,24a-dodecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,24aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.

RN 186959-54-6 HCAPLUS

CN 14H-Pyrido[2,1-c][1,10,4]dioxaazacycloeicosine-1,7,14,17,18(8H,20H)-pentone, 3,4,5,6,11,12,15,16,21,22,23,23a-dodecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,23aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.

KATHLEEN FULLER EIC1700 308-4290

RN 186959-57-9 HCAPLUS

CN 15,18-Epoxy-14H-pyrido[2,1-c][1,12,4]dioxaazacyclodocosine-1,7,14,19,20(8H,22H)-pentone, 3,4,5,6,11,12,15,16,17,18,23,24,25,25atetradecahydro-4,10,18-trimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,15S,18R,25aS)- (9CI) (CA INDEX NAME)

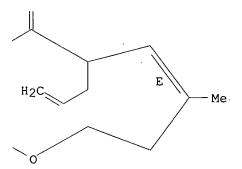
Absolute stereochemistry. Double bond geometry as described by E or Z.

PAGE 1-A

PAGE 1-B

0

PAGE 2-B



KATHLEEN FULLER EIC1700 308-4290

RN 186959-60-4 HCAPLUS

CN 16,19-Epoxy-3H,15H-pyrido[2,1-c][1,12,4]dioxaazacyclotricosine-1,7,15,20,21(4H,23H)-pentone, 5,6,8,11,12,13,16,17,18,19,24,25,26,26atetradecahydro-4,10,19-trimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,16S,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by E or Z.

PAGE 1-A

PAGE 1-B

PAGE 2-B

KATHLEEN FULLER EIC1700 308-4290

RN 186959-61-5 HCAPLUS

CN 17,20-Epoxy-16H-pyrido[2,1-c][1,12,4]dioxaazacyclotetracosine-1,7,16,21,22(8H,24H)-pentone, 3,4,5,6,11,12,13,14,17,18,19,20,25,26,27,27ahexadecahydro-4,10,20-trimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,17S,20R,27aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 186959-64-8 HCAPLUS

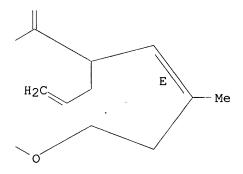
CN 15,18-Epoxy-14H-pyrido[2,1-c][1,12,4]dioxaazacyclodocosine-1,7,14,19,20(8H,22H)-pentone, 3,4,5,6,11,12,15,16,17,18,23,24,25,25atetradecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,15S,18R,25aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by E or Z.

PAGE 1-A

PAGE 1-B

PAGE 2-B



RN 186959-67-1 HCAPLUS

CN 16,19-Epoxy-3H,15H-pyrido[2,1-c][1,12,4]dioxaazacyclotricosine-1,7,15,20,21(4H,23H)-pentone, 5,6,8,11,12,13,16,17,18,19,24,25,26,26atetradecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,16S,19R,26aS)- (9CI) (CA·INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by  ${\tt E}$  or  ${\tt Z}$ .

PAGE 1-A

PAGE 1-B

PAGE 2-B

RN 186959-70-6 HCAPLUS

CN 17,20-Epoxy-16H-pyrido[2,1-c][1,12,4]dioxaazacyclotetracosine-1,7,16,21,22(8H,24H)-pentone, 3,4,5,6,11,12,13,14,17,18,19,20,25,26,27,27ahexadecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,17S,20R,27aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 186959-77-3 HCAPLUS

CN 3H-4,8-Methenopyrido[2,1-c][1,9,4]dioxaazacyclopentacosine-1,9,18,22,23(25H)-pentone, 10,11,12,13,14,15,16,17,20,21,26,27,28,28atetradecahydro-21,21-dimethyl-3-(2-phenylethyl)-, (28aS)- (9CI) (CA INDEX NAME)

RN 186974-30-1 HCAPLUS

CN 3H-4,8-Metheno-10H-pyrido[2,1-c][1,9,17,4]trioxaazacyclotricosine-1,16,20,21(11H,23H)-tetrone, 12,13,14,15,18,19,24,25,26,26a-decahydro-19,19-dimethyl-3-(2-phenylethyl)-, (3R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 252002-64-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-(4-methoxyphenyl)butyl ester (9CI) (CA INDEX NAME)

MeO 
$$\begin{array}{c|c} \cdot & \circ \\ \cdot & \circ \\ \text{CH2) 4-O-C} \\ \text{Ph-C-C} \\ \parallel & \parallel \\ \circ & \circ \\ \end{array}$$

RN 252002-66-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

RN 252002-68-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 3-(3-pyridinyl)propyl ester (9CI) (CA INDEX NAME)

RN 252002-79-2 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 4-(4-methoxyphenyl)butyl ester (9CI) (CA INDEX NAME)

RN 252002-81-6 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-cyclohexylpropyl ester (9CI) (CA INDEX NAME)

RN 252002-83-8 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

RN 252002-96-3 HCAPLUS

CN 14H-Pyrido[2,1-c][1,12,4]dioxaazacyclodocosine-1,7,14,19,20(8H,22H)-pentone, 3,4,5,6,11,12,15,16,17,18,23,24,25,25a-tetradecahydro-4,10-dimethyl-8-(2-propenyl)-3-[2-(3-pyridinyl)ethyl]-, (3R,4R,9E,25aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by E or Z.

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ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2001 ACS
L15
AN.
     1998:804155 HCAPLUS
DN
     130:52725
     Preparation and use of pyrrolidines in hair growth compositions
ΤI
IN
     Hamilton, Gregory S.; Steiner, Joseph P.
PA
     Guilford Pharmaceuticals Inc., USA
SO
     PCT Int. Appl., 187 pp.
     CODEN: PIXXD2
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     34-2 (Amino Acids, Peptides, and Proteins)
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KATHLEEN FULLER EIC1700 308-4290

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GI
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$$\begin{array}{c|c}
 & n \\
 & N \\$$

This invention relates to pharmaceutical compns. and methods for treating alopecia and promoting hair growth using non-immunosuppressive neuroimmunophilin FKBP ligands [I; n = 1, 2, 3; Y = CO, COCO, SO2, CS; X = O, S; Z = S, O, CH2, (CH2)3, SCH2, S(CH2)2, S(CH2)3; R1 = benzyl, 3-phenylpropyl, 3-(3-pyridyl)propyl, diphenylmethyl, etc.; R2 = cyclohexyl, Ph, tert-Bu, 3,4,5-trimethoxyphenyl, etc.], stereoisomers, pharmaceutically acceptable salts, esters, and solvates thereof. The title compd. II was tested, in vitro, in inhibition of the peptidyl-prolyl isomerase activity and preferably for use topically to the skin to treat alopecia or promote hair growth effectively.

II

ST carboxylate pyrrolidine prepn alopecia treatment

IT Alopecia

Drug delivery systems

(prepn. and use of pyrrolidines in hair growth compns.)

IT 186452-09-5P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and use of pyrrolidines in hair growth compns.) ΙT 186268-51-9P 186268-52-0P 186268-50-8P 186268-53-1P 186268-54-2P 186268-58-6P 186268-56-4P 186268-57-5P 186268-63-3P 186268-64-4P 186268-65-5P 186268-67-7P 186268-66-6P 186268-68-8P 186452-05-1P 186452-07-3P 186452-08-4P 186452-10-8P 186452-11-9P 186452-06-2P 186452-13-1P 186452-14-2P 186452-15-3P 186452-16-4P 186452-12-0P 186452-17-5P 186452-18-6P 186452-19-7P 186452-20-0P 205388-13-2P 205388-15-4P 205388-14-3P 205388-16-5P 205388-18-7P 205388-19-8P 205388-22-3P 205388-24-5P 205388-20-1P 205388-21-2P 205388-23-4P

KATHLEEN FULLER EIC1700 308-4290

205388-28-9P

205388-29-0P

205388-27-8P

205388-25-6P

.205388-26-7P

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205388-33-6P
     205388-30-3P
                    205388-31-4P
                                    205388-32-5P
                                                                  205388-34-7P
                                    205388-37-0P
                                                   205388-38-1P
                                                                  205388-39-2P
                    205388-36-9P
     205388-35-8P
                                    205388-43-8P
                                                                  205388-47-2P
                                                   205388-44-9P
     205388-41-6P
                    205388-42-7P
                                                   205388-53-0P
                                    205388-50-7P
     205388-48-3P
                    205388-49-4P
                                                   205388-57-4P
     205388-54-1P
                    205388-55-2P
                                    205388-56-3P
                                                                  205388-63-2P
                                    205388-61-0P
                                                   205388-62-1P
     205388-58-5P
                    205388-59-6P
                                    205448-80-2P
                                                   210048-08-1P
                                                                  210048-10-5P
     205388-80-3P
                    205448-79-9P
                                    210048-13-8P
                                                   210048-14-9P
                                                                  210048-15-0P
     210048-11-6P
                    210048-12-7P
                                    210048-18-3P
                                                   210048-19-4P
                                                                  210048-20-7P
     210048-16-1P
                    210048-17-2P
                                    210048-23-0P
                                                   210048-25-2P
                    210048-22-9P
                                                                  210103-54-1P
     210048-21-8P
                                    212762-79-3P
                                                   217178-10-4P
                                                                  217179-46-9P
     210103-55-2P
                    210103-60-9P
                                   217180-57-9P
                                                   217180-59-1P
                    217180-44-4P
     217179-50-5P
                    217186-43-1P
                                    217186-45-3P
                                                   217186-46-4P
     217180-90-0P
                    217186-49-7P
                                    217186-50-0P
                                                   217186-51-1P
                                                                  217186-52-2P
     217186-47-5P
     217186-53-3P
                    217186-54-4P
                                   217186-55-5P
                                                   217186-56-6P
                                                                  217186-57-7P
     217186-58-8P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and use of pyrrolidines in hair growth compns.)
                                            96-15-1, 2-Methylbutylamine
ΙT
     86-81-7, 3,4,5-Trimethoxybenzaldehyde
     103-63-9, 2-(Bromoethyl)benzene 108-98-5, Phenyl mercaptan, reactions
     122-97-4, 3-Phenyl-1-propanol
                                     558-13-4, Carbontetrabromide
                                                                     955-40-8
     1122-82-3, Cyclohexylisothiocyanate
                                           2577-48-2, L-Proline methyl ester
     2859-67-8, 3-Pyridinepropanol 4830-93-7, 1-Chloro-4-phenylbutane
     5406-18-8, 3-(p-Methoxyphenyl)-1-propanol
                                                 5781-53-3, Methyloxalyl
                20329-96-8, Methyl (E)-3,4,5-Trimethoxycinnamate
                                                                    26250-84-0
     28276-08-6, 1,1-Dimethylpropylmagnesium chloride
                                                        32559-18-5, Methyl
     pipecolate hydrochloride
                                34592-47-7
                                              53560-26-2
     RL: RCT (Reactant)
        (prepn. and use of pyrrolidines in hair growth compns.)
                                      17486-86-1P, 1,5-Diphenyl-3-pentanol
ΙT
     104-53-0P, 3-Phenyl-1-propanal
                                 69603-49-2P, 3-Pyridinepropanethiol
     21011-66-5P
                   57293-19-3P
                                                 186268-77-9P
     88537-44-4P
                   89113-44-0P
                                 139419-63-9P
                                                                186268-78-0P
     205388-66-5P
                    205388-67-6P
                                    205388-68-7P
                                                   205448-82-4P
                                                                  210048-37-6P
                                                   217186-09-9P
     210048-38-7P
                    210103-98-3P
                                    210103-99-4P
                                                                  217186-59-9P
                    217186-61-3P
                                   217186-62-4P
     217186-60-2P
                                                   217186-63-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and use of pyrrolidines in hair growth compns.)
RE.CNT
RE
(1) Ariad Gene Therapeutics, Inc; WO 9731898 A 1997 HCAPLUS
(2) Hamilton, G; US 5614547 A 1997 HCAPLUS
(3) The Board of Trustees of the Leland Stanford Junior Univ; WO 9502684 A 1995
    HCAPLUS
TT
     205388-48-3P 205388-54-1P 217179-50-5P
     217180-90-0P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and use of pyrrolidines in hair growth compns.)
RN
     205388-48-3 HCAPLUS
     2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-(2-phenylethyl)
CN
     ester (9CI) (CA INDEX NAME)
```

FILE

RN 205388-54-1 HCAPLUS

CN 2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-[3-(4-methoxyphenyl)propyl] ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & \\ & & & & & & \\ \text{MeO} & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & \\ & & \\ &$$

RN 217179-50-5 HCAPLUS

CN 2-Piperidinecarbothioic acid, 1-(oxophenylacetyl)-, S-[3-phenyl-1-(2-phenylethyl)propyl] ester (9CI) (CA INDEX NAME)

O O 
$$\| \| \|$$
  $C-C-Ph$   $C-S-CH-CH_2-CH_2-Ph$   $\| \|$   $C-CH_2-CH_2-Ph$   $C-CH_2-CH_2-Ph$ 

RN 217180-90-0 HCAPLUS

CN Piperidine, 1-(cyclohexyloxoacetyl)-2-(1-oxo-6-phenylhexyl)- (9CI) (CA INDEX NAME)

L15 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:738370 HCAPLUS

DN 128:43577

TI Topical FK506: a potent immunotherapy for alopecia areata? Studies using the Dundee experimental bald rat model

KATHLEEN FULLER EIC1700 308-4290

```
ΑU
     Mcelwee, K. J.; Rushton, D. H.; Trachy, R.; Oliver, R. F.
CS
     Department of Biological Sciences, University of Dundee, Dundee, DD1 4HN,
     UK
SO
     Br. J. Dermatol. (1997), 137(4), 491-497
     CODEN: BJDEAZ; ISSN: 0007-0963
PB
     Blackwell
DT
     Journal
LĄ
     English
CC
     1-7 (Pharmacology)
AΒ
     We elected to examine the efficacy of the topically applied
     immunosuppressive agent FK506 (Prograf) in the treatment of alopecia
     areata (AA) using the Dundee exptl. bald rat (DEBR) model. Thirty
     lesional DEBR rats were allocated to five groups of six. Group I rats
     received 0.1 mL of a 0.25% soln. of FK506 within a 2.times.2 cm marked
     area on one bald flank twice a week (125 .mu.g FK506/cm2 per wk) for 8 wk,
    while the contralateral flank was left untreated. In group II, 0.05 mL of
     a 0.1% soln. of FK506 was applied 5 days per wk on one flank (62.5 .mu.g
     FK506/cm2 per wk) and control vehicle to the opposite flank for 8 wk.
     Group III rats were treated as in group II except that drug and vehicle
    were applied twice a week (25 .mu.g FK506/cm2 per wk) for 4 wk. A pos.
     control group received orally administered cyclosporin A (CsA) (10 mg/kg
     daily) for 8 wk and a further group was left untreated. Rats were
    regularly examd. and photographed with skin biopsies taken from groups II
 is and III. All FK506-treated rats regrew hair at the site of drug
    application within 14-21 days. Growth continued for 3 wk beyond
    termination of treatment after which gradual hair loss was obsd.
     growth was seen as a result of vehicle application and hair loss continued
    on untreated areas and in the untreated control group. Immunohistol.
    revealed a drastic redn. in the follicular inflammatory infiltrate at the
     site of the FK506 application. The oral CsA group responded by
     simultaneous regrowth of hair over the whole body. Our findings suggest
23
    that FK506 may have considerable potential as a topical treatment for AA.
ST
    FK506 topical alopecia areata
TΨ
    Alopecia
        (areata; topical FK506 for treatment of alopecia areata)
TΤ
    {\tt Immunosuppressants}
     Topical drug delivery systems
        (topical FK506 for treatment of alopecia areata)
IT
    104987-11-3, FK506
    RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
    effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
    USES (Uses)
        (topical FK506 for treatment of alopecia areata)
    104987-11-3, FK506
    RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (topical FK506 for treatment of alopecia areata)
    104987-11-3
RN
                 HCAPLUS
     15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
     tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
    dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
    methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,
     (3S, 4R, 5S, 8R, 9E, 12S, 14S, 15R, 16S, 18R, 19R, 26aS) - (9CI) (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

L15 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:269212 HCAPLUS

DN 126:312233

TI Hair growth modulation by topical immunophilin ligands: induction of anagen, inhibition of massive catagen development, and relative protection from chemotherapy-induced alopecia

AU Maurer, Marcus; Handjiski, Bori; Paus, Ralf

CS Department of Dermatology, Charite Hospital, Humboldt-Universitat zu Berlin, Berlin, D-10117, Germany

SO Am. J. Pathol. (1997), 150(4), 1433-1441 CODEN: AJPAA4; ISSN: 0002-9440

PB American Society for Investigative Pathology

DT Journal

AB

LA English

CC 1-12 (Pharmacology)

Selected immunophilin ligands (IPLs) are not only potent immunosuppressants but also modulate hair growth. Their considerable side effects, however, justify at best topical applications of these drugs for the management of clin. hair growth disorders. Therefore, the authors have explored hair growth manipulation by topical cyclosporin A (CsA) and FK 506 in previously established murine models that mimic premature hair follicle regression (catagen) or chemotherapy-induced alopecia, two major pathomechanisms underlying human hair loss. The authors confirm that topical CsA and FK 506 induce active hair growth (anagen) in the back skin of C57BL/6 mice with all follicles in the resting stage (telogen) and show that both IPLs also inhibit massive, dexamethasone-induced, premature catagen development in these mice. Furthermore, the authors demonstrate that CsA and FK 506 provide relative protection from alopecia and follicle dystrophy induced by cyclophosphamide, possibly by favoring the dystrophic anagen pathway of follicle response to chem. damage. Although it remains to be established whether these IPLs exert the same effects on human hair follicles, the authors study provides proof of the principle that topical IPLs can act as potent manipulators of clin. relevant hair-cycling pathomechanisms. This strongly encourages one to explore the use of topical IPLs in the management of human hair growth disorders.

ST hair growth stimulation topical immunophilin ligand; chemotherapy alopecia prevention topical immunophilin ligand; cyclosporin A hair growth stimulation; FK506 hair growth stimulation

IT Alopecia

Antitumor agents

Hair growth stimulants

(hair growth modulation by topical immunophilin ligands cyclosporin A and FK 506 in relation to induction of anagen and inhibition of massive catagen development and relative protection from chemotherapy-induced alopecia)

IT Immunophilins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ligands; hair growth modulation by topical immunophilin ligands cyclosporin A and FK 506 in relation to induction of anagen and inhibition of massive catagen development and relative protection from chemotherapy-induced alopecia)

IT 50-18-0, Cyclophosphamide

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (hair growth modulation by topical immunophilin ligands cyclosporin A and FK 506 in relation to induction of anagen and inhibition of massive catagen development and relative protection from chemotherapy-induced alopecia)

IT 59865-13-3, Cyclosporin A 104987-11-3, FK506

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hair growth modulation by topical immunophilin ligands cyclosporin A and FK 506 in relation to induction of anagen and inhibition of massive catagen development and relative protection from chemotherapy-induced alopecia)

IT **104987-11-3**, FK506

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hair growth modulation by topical immunophilin ligands cyclosporin A and FK 506 in relation to induction of anagen and inhibition of massive catagen development and relative protection from chemotherapy-induced alopecia)

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

```
L15 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ΑN
     1996:597898 HCAPLUS
DN
     125:238612
     Effects of potent immunotherapies, oral cyclosporin A and topical FK506 in
TΤ
     the DEBR rat model for alopecia areata
     McElwee, K. J.; Lowe, J. G.; Oliver, R. F.
ΑU
     Department Biomedical Sciences, University Dundee, UK
CS
     Int. Congr. Ser. (1996), 1111 (Hair Research for the Next Millenium),
SO
    259-263
     CODEN: EXMDA4; ISSN: 0531-5131
     Journal
DT
LA
     English
     1-12 (Pharmacology)
CC
     Section cross-reference(s): 63
     The effect of immunosuppressant therapy with oral cyclosporin A and
AΒ
     topical FK506 on alopecia areata was studied in the DEBR rat model.
     oral cyclosporin topical FK506 alopecia areata; immunosuppressant
ST
     cyclosporin FK506 alopecia areata
IT
     Immunosuppressants
        (immunosuppressant therapy with oral cyclosporin A and topical FK506
        effect on alopecia areata in DEBR rat model)
IT
    Alopecia
        (areata, immunosuppressant therapy with oral cyclosporin A and topical
        FK506 effect on alopecia areata in DEBR rat model)
     Pharmaceutical dosage forms
TT
        (topical, FK506; immunosuppressant therapy with oral cyclosporin A and
        topical FK506 effect on alopecia areata in DEBR rat model)
     59865-13-3, Cyclosporin A 104987-11-3, FK506
TT
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immunosuppressant therapy with oral cyclosporin A and topical FK506
        effect on alopecia areata in DEBR rat model)
     104987-11-3, FK506
ΙT
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immunosuppressant therapy with oral cyclosporin A and topical FK506
        effect on alopecia areata in DEBR rat model)
RN
     104987-11-3 HCAPLUS
     15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
CN
     tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
     dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-,
     (3S, 4R, 5S, 8R, 9E, 12S, 14S, 15R, 16S, 18R, 19R, 26aS) - (9CI)
                                                           (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

FILE

L15 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:460554 HCAPLUS

DN 122:230322

TI Effects of immunosuppressive peptidyl-prolyl cis-trans isomerase (PPIase) inhibitors, cyclosporin A, FK506, ascomycin and rapamycin, on hair growth initiation in mouse: Immunosuppression is not required for new hair growth

AU Iwabuchi, Tokuro; Maruyama, Tadashi; Sei, Yoshihiro; Adachi, Kenji

CS Kamaishi Laboratories, Marine Biotechnology Institute, Kamaishi, 026, Japan

SO J. Dermatol. Sci. (1995), 9(1), 64-9 CODEN: JDSCEI; ISSN: 0923-1811

DT Journal

LA English

CC 1-7 (Pharmacology)

AB The effects of immunosuppressive peptidyl-prolyl cis-trans isomerase (PPIase) inhibitors, cyclosporin A, FK506, ascomycin and rapamycin, on hair growth initiation (anagen hair induction) in mouse were studied by topical application on the dorsal skin surface during the telogen phase of the hair cycle. Single applications of cyclosporin A and FK506 (10 to 100 nmol in 5 .mu.L of ethanol) induced new hair growth in 12 days within the restricted area where the compds. were applied. On the other hand, ascomycin and rapamycin did not initiate new anagen hairs even at higher doses (1 .mu.mol in 5 to 10 .mu.L of ethanol). The effects of simultaneous application of the immunosuppressants were also tested by a single topical application. Ascomycin did not inhibit the anagen hair induction by cyclosporin A, but inhibited hair induction by FK506. Rapamycin inhibited new hair growth induced by cyclosporin A and FK506. These results suggest that the inhibition of PPIase is not required for the initiation of a new hair cycle in mice, and that anagen hair induction caused by cyclosporin A and FK506 is not a result of immunosuppression. The present results also indicate that a single application of an adequate quantity of cyclosporin A and FK506 is sufficient to initiate new hair arowth.

ST immunosuppressant peptidylprolyl isomerase hair growth

IT Hair

Immunosuppressants

(immunosuppressive peptidyl-prolyl cis-trans isomerase inhibitor effect on hair growth initiation)

IT 53123-88-9, Rapamycin 59865-13-3, Cyclosporin A 104987-11-3, FK506 104987-12-4, Ascomycin KATHLEEN FULLER EIC1700 308-4290

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (immunosuppressive peptidyl-prolyl cis-trans isomerase inhibitor effect on hair growth initiation)

IT 95076-93-0, Peptidyl-prolyl cis-trans isomerase

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(immunosuppressive peptidyl-prolyl cis-trans isomerase inhibitor effect on hair growth initiation)

IT 53123-88-9, Rapamycin 104987-11-3, FK506

104987-12-4, Ascomycin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (immunosuppressive peptidyl-prolyl cis-trans isomerase inhibitor effect on hair growth initiation)

RN 53123-88-9 HCAPLUS

CN Rapamycin (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 2-A

Мe

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

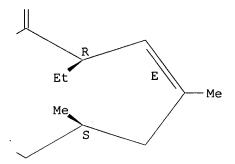
RN 104987-12-4 HCAPLUS
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)tetrone, 8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26ahexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as described by E or Z.

PAGE 1-A

PAGE 1-B

PAGE 2-B



L15 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1994:644746 HCAPLUS

DN 121:244746

TI Hair growth-stimulating effects of cyclosporin A and FK506, potent immunosuppressants

AU Yamamoto, Satoshi; Kato, Ryuichi

CS Sch. Med., Keio Univ., Tokyo, 160, Japan

SO J. Dermatol. Sci. (1994), 7(Suppl.), S47-S54

CODEN: JDSCEI; ISSN: 0923-1811

DT Journal; General Review

LA English

AΒ

CC 1-0 (Pharmacology)

A review with 87 refs. Cyclosporin A (CsA), a cyclic endecapeptide, is a T cell-specific immunosuppressant and is successfully used in the field of organ transplantation. Another T cell-specific immunosuppressant, FK506, a more recently discovered macrolide antibiotic, is effective against graft rejection at much lower doses than CsA. Although totally different in structure, both compds. inhibit T cell activation by interfering with the prodn. of interleukin-2 (IL-2) by inhibiting IL-2 gene expression, probably through the inhibition of calcineurin, a Ca2+/calmodulindependent phosphatase. Clin. studies have revealed that FK506 induces a variety of side effects in common with CsA. One of the most common side effects of CsA is hypertrichosis. The hair growth stimulating effect of CsA is obsd. not only in normal but also in pathol. conditions of hair growth, i.e. in patients with alopecia areata and also in some patients with male-pattern alopecia. Although hypertrichosis is induced by both topical and oral administration of CsA, there has been no report showing that FK506 induces hypertrichosis. Recently we have found that topical application of FK506 to skins of mice, rats and hamsters markedly stimulates hair growth. This hair growth stimulating effect of FK506 is obsd. when applied topically but not by oral administration, even with a dose which causes marked immunosuppression. The hair growth stimulating effect of FK506 in normal animals may apparently be unrelated to its immunosuppressive effect. In vitro studies revealed that FK506 directly stimulates hair follicles. Mechanisms of hair growth stimulating effects of FK506 and CsA remain to be elucidated. Although at present it is not clear whether FK506 stimulates hair growth in humans, potential use of FK506 for therapeutic purposes as a stimulate of hair growth is anticipated.

ST review hair growth cyclosporin FK506 immunosuppressant

IT Hair

Hirsutism

Immunosuppressants

(hair growth-stimulating effects of immunosuppressants cyclosporin A and FK506)

IT 59865-13-3, Cyclosporin A 104987-11-3, FK506

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

KATHLEEN FULLER EIC1700 308-4290

(hair growth-stimulating effects of immunosuppressants cyclosporin A and FK506)  $\,$ 

IT 104987-11-3, FK506

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hair growth-stimulating effects of immunosuppressants cyclosporin A and FK506)

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

L15 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2001 ACS

AN 1994:260813 HCAPLUS

DN 120:260813

TI Stimulation of hair growth by topical application of FK506, a potent immunosuppressive agent

AU Yamamoto, Satoshi; Jiang, Hong; Kato, Ryuichi

CS Sch. Med., Keio Univ., Tokyo, 160, Japan

SO J. Invest. Dermatol. (1994), 102(2), 160-4

CODEN: JIDEAE; ISSN: 0022-202X

DT Journal

LA English

CC 1-7 (Pharmacology)

FK506, a macrolide antibiotic produced by Streptomyces tsukubaensis, is known as a potent T cell - specific immunosuppressant, and is effective against graft rejection after organ transplantation. Topical application of FK506 (0.03-1 .mu.mol) to dorsal skin of CD-1 mice stimulated hair growth in a dose-dependent manner. Unlike topical application, oral administration of 30 mg/kg of FK506, a dose that induces marked immunosuppression, did not stimulate significant hair growth. Topical application of FK506 also stimulated hair growth of rats and Syrian golden hamsters. FK506 stimulated hair growth even in SCID mice that lack both B- and T-cell immunity. Therefore, it is unlikely that the hair growth stimulatory effect of FK506 results from its immunosuppressant effect. FK506 (0.01-1 .mu.M) stimulated both [3H]thymidine and [3H]glycine uptakes KATHLEEN FULLER EIC1700 308-4290

to cultured mouse vibrissae follicles in a concn.-dependent manner. Moreover, when the follicles were treated with FK506 (1 .mu.M) for 16 d, the size of the follicles (length of hair plus follicle) increased slightly but significantly. The size of the non-treated follicles did not increase significantly. These results indicate that FK506 directly stimulates hair follicles. Long-term treatment of mice with FK506, i.e., topical application of 1 .mu.mol FK506 twice a week for 6 mo, did not affect body wt. gain of mice, and the FK506-treated mice looked healthy. FK506 may be useful as a stimulant of hair growth.

ST hair growth stimulation FK506 topical administration

IT Hair

(growth of, FK506 topical administration stimulation of)

IT 104987-11-3, FK506

RL: BIOL (Biological study)

(hair growth stimulation by topical administration of)

IT 104987-11-3, FK506

RL: BIOL (Biological study)

(hair growth stimulation by topical administration of)

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

- L15 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2001 ACS
- AN 1992:75962 HCAPLUS
- DN 116:75962
- ${\tt TI}$  Differential effects of FK 506 and cyclosporine on hair regrowth in the DEBR model of alopecia areata
- AU Sainsbury, T. S. L.; Duncan, J. I.; Whiting, P. H.; Hewick, D. S.; Johnson, B. E.; Thomson, A. W.; Oliver, R. F.
- CS Dep. Pathol., Univ. Aberdeen, Aberdeen, AB9 2ZD, UK
- SO Transplant. Proc. (1991), 23(6), 3332-4 CODEN: TRPPA8; ISSN: 0041-1345
- DT Journal
- LA English
- CC 1-7 (Pharmacology)

AB In the Dundee exptl. bald rat (DEBR) model of slopecia areata, FK 506 appeared to be more toxic than CyA, was less effective in down-regulating the cutaneous inflammatory infiltrate, and was assocd. with only marginal hair growth. As yet, neither drug has been assessed topically in the DEBR. Undoubtedly, the topical application of an effective formulation of CyA or FK 506 for the treatment of alopecia areata would be desirable since drug-induced systemic toxicity could be minimized.

ST alopecia cyclosporin FK506 hair growth

IT Immunosuppressants

(hair regrowth response to, in Dundee exptl. bald rat model of alopecia areata)

IT Alopecia

(areata, cyclosporin A and FK506 effect on hair regrowth and Dundee exptl. bald rat model of)

IT 59865-13-3, Cyclosporin A 104987-11-3, FK506

RL: BIOL (Biological study)

(hair regrowth response to, in Dundee exptl. bald rat model of alopecia areata)

IT 104987-11-3, FK506

RL: BIOL (Biological study)

(hair regrowth response to, in Dundee exptl. bald rat model of alopecia areata)

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

- L15 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2001 ACS
- AN 1991:520057 HCAPLUS
- DN 115:120057
- TI Hair growth stimulant compositions containing tricyclic compounds
- IN Honbo, Toshiyasu; Hata, Takehisa; Ishino, Akihiro; Tsuji, Yoshiharu
- PA Fujisawa Pharmaceutical Co., Ltd., Japan
- SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English
IC ICM A61K007-06
CC 63-6 (Pharmaceuticals)
FAN CNT 1

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AB A hair grwoth stimulant compn. contains the tricyclic compds. [I; R1-6 = H, forms another bond with a C atom to which it is bonded (R2 may be an alkyl group); R7 = H, OH, alkoxy, etc.; R8-9 = H, OH; R10 = H, alkyl, etc.; X = oxo group or -CH2O-; Y = oxo group, HNR11R12, HOR13; R11-12 = H, alkyl, aryl, tosyl; R13-19, R22-23 = H or alkyl; R20-21 = oxo group or other defined groups; n = 1-3] or its pharmaceutically acceptable salts as active ingredient. I have excellent hair growth stimulant effect on male pattern alopecia and senile alopecia. A lotion contained 95% EtOH 80.0, FK-506 10.0 .alpha.-tocopherol acetate 0.01, ethoxylated hardened castor oil 0.5, purified water 9.0% and perfume and dye q.s. The lotion was coated once or twice/day, 5 mL each time, at a site of baldness or alopecia.

Ι

ST tricyclic compd hair growth stimulant; FK506 hair growth stimulant lotion; alopecia baldness tricyclic compd

IT Shampoos

(FK-506 or related compds. in, as hair growth stimulants)

IT Hair preparations

(creams, FK-506 or related compds. in, as hair growth stimulants)
KATHLEEN FULLER EIC1700 308-4290

IT Hair preparations
(growth stimulants, emulsions, FK-506 or related compds. in, as hair growth stimulants)

IT Hair preparations

(liqs., FK-506 or related compds. in, as hair growth stimulants)

IT Hair preparations

(lotions, FK-506 or related compds. in, as hair growth stimulants)

IT Alopecia

(male pattern, treatment of, with hair growth stimulant prepn. contg. FK-506 and related tricyclic compds.)

IT Alopecia

(senile, treatment of, with hair growth stimulant prepn. contg. FK-506 and related tricyclic compds.)

IT Hair preparations

(tonics, FK-506 or related compds. in, as hair growth stimulants)

IT **104987-11-3**, FK-506

RL: BIOL (Biological study)

(hair growth stimulant prepn. contg., for treating male pattern alopecia or senile alopecia)

IT **104987-11-3**, FK-506

RL: BIOL (Biological study)

(hair growth stimulant prepn. contg., for treating male pattern alopecia or senile alopecia)

RN 104987-11-3 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.